EXHIBIT 32

Food and Drug Administration Office of Regulatory Affairs
Collection Report
For Sample Number: 377410

This is an accurate reproduction of the original electronic record as of 02/12/2007

MR 2/13/07

Flag		Flag Remarks			
Survey Sample		Finished Product CDER Survey 2007-057			
Episode Number	**Origin**	**Basis**	**Sample Type**	**FIS Smpl Num**	**Status**
	Domestic	Surveillance	Official	0768704	Completed
FEI	**Date Collected**	**Product Code**	**Responsible Firm**	**PAC**	**Hours**
2244683	02/09/2007	63FCA06	Manufacturer	56008A	8
Compliance Num	**Country of Origin**				
	United States				
Related Smpl Num	**Position Class**	**Sampling District**	**NDC Number**	**Permit Number**	**Storage Rqrmnt.**
	INV	NWJ-DO	52152-145		Ambient
Dealer is Consumer	**Crx/DEA Schedule**	**Recall Num**	**Consumer Compl. Num**	**Brand Name**	
No				Digitek	

Product Description
digoxin tablets, .0125 mg

Product Label
Each bottle labeled in part: "**NDC 62794-145-01 DIGITEK, (digoxin tablets, USP) 125 mcg (.0125 mg), 100 TABLETS, Rx Only**"

Reason for Collection	MFG Codes	Expiration Date
Sample was collected as per FACTS Assignment # 794297, OperationID # 3101179, FY 2007 Finished Product CDER Survey 2007-057.	70078A1	JAN 09

Firm Legal Name	Address	Type of Firm	Firm FEI	FCE
Actavis Totowa LLC	101 E Main St Little Falls, NJ 07424-5608 US	Manufacturer	2244683	
Actavis Totowa LLC	4 Taft Rd Totowa, NJ 07512-1006 US	Dealer	3003450194	

Size of Lot	Est. Value	Rcpt Type	Carrier Name	Date Shipped
(b) (4) bottles of 100 count each	$ (b) (4)	FDA484		

Description of Sample
Two 100-count bottles of digoxin tablets (.0125 mg).

Method of Collection
See continuation.

How Prepared
See continuation

Collector's Identification on Package and/or Label
"377410 KAZ 2/9/07"

Collector's Identification on Seal
"377410 Kristy A. Zielny 2/9/07"

Sample Delivered To
FEDEX pick-up at NBRP

Date Delivered	Orig C/R & Records To
02/12/2007	NWJ-DO
Lab w/Split Sample	**Lab**
0	DEN-LAB

Document Number	Document Date	Document Type	Document Remarks
Att. 1	02/09/2007	Other	FDA 482, Notice of Inspection, 1 page
Att. 2	02/09/2007	Other	FDA 484, Receipt for Samples, 1 page
Att. 3	02/09/2007	Other	Certificate of Analysis for Lot # 70078A
Att. 4	04/02/2002	Other	Methods of Analysis, 16 pages

DEFENDANT'S EXHIBIT 32

Food and Drug Administration Office of Regulatory Affairs
Collection Report
For Sample Number: 377410

This is an accurate reproduction of the original electronic record as of 02/12/2007

Remarks
See continuation.

Payment Amount	Payment Method	704(d) Sample	702(b) Portion	Collector's Name
$0.00	No Charge	No	No	Kristy A Zielny

Name of Signer	Date & Time of Signature	Meaning
Kristy A Zielny	02/12/2007 07:53 AM ET	Collector

Continuation:

Method of Collection
Two 100-count bottles of digoxin tablets, USP (.125 mg) were selected from the firm's inventory of Lot # 70078A1. The sample was identified and officially sealed on 2/9/07.

How Prepared
Sample # 377410 consists of two identical subsamples. The subs were identified as stated above and the sample was officially sealed at the firm on 2/9/07. The sample was then transported to NBRP, where it was stored in the locked sample room until shipment.

Remarks
All methods are compendial and follow USP 29-NF24, page 704, Digoxin Tablets Monograph, with the exception of Impurity testing, which involves two in-house methods. The first in-house method is the "Limit test for related glycoside as Digoxigenin & Digoxigenin bisdigitoxoside" which utilizes relative retention times. The second in-house method is the "Limit test for related glycoside as Gitoxin", for which the reference standard is a USP standard for Gitoxin.

The NDC number for this product is 52152-145. This is Amide's NDC number for the product (the NDC #s are currently listed under Amide and are in the process of being changed over to Actavis). The NDC number that appears on the labeling of this product, 62794-145-01 is the distributor's NDC number, namely Bertek Pharmaceuticals, Inc.

FLAG:

ANALYST WORKSHEET	1. PRODUCT: Digoxin tablets, USP 125µg	2. SAMPLE NUMBER: 377410
3. SEALS: ☒ INTACT ☐ BROKEN ☐ NONE	4. DATE RECEIVED: 4-9-07	5. RECEIVED FROM: Gianna R Costo
		6. DISTRICT OR LAB: DEN-DO

7. DESCRIPTION OF SAMPLE

One large whirl-pak bag officially sealed "377410 2/8/07 Kristy A. Zielny" containing two intact bottles of product identified "SAMPLE # 377410 2/9/07 KAZ" and "Sub # 1" or "Sub # 2" respectively.
Note: C/R states Collector's ID on Seal "377410 Kristy A. Zielny 2/9/07"
Note: C/R states Product Description & Product Label "....0125mg...". (125µg = 0.125mg)
FDA525, sample package identification, contains a product certificate of analysis continued next page

8. NET CONTENTS			9. LABELING	
☐ NOT APPLICABLE	DECLARE/UNIT: 100 tablets		1	ORIGINAL(S) SUBMITTED
☒ NOT DETERMINED	AMOUNT FOUND:		1	COPIES SUBMITTED
___ UNITS EXAMINED	% OF DECLARED:		☐	NONE

10. SUMMARY OF ANALYSIS

CONTAINER: Opaque white plastic cylindrically shaped bottle with knurled safety cap and addition safety seal underneath. ~ dimensions: 7½cm high x 4cm diameter.

LABELING: Multicolored paper stick-on label and product insert.

CODE: "Control No.: 70078A1 Exp. Date: JAN 09"

PRODUCT: Tablet: round top view, flat side view, solid light yellow, plain on one side, scored on the other side with embossed writing "B" on the top and "145" on the bottom. ~ dimensions: 6mm in diameter x 2mm high.

ANALYSIS: Assay, Content Uniformity, Dissolution, Organic Volatile Impurities

METHOD: All analyses by "Digoxin Tablets" USP on-line official → 11/30/07.
Note: C/R calls for impurity testing for related glycosides utilizing two in-house methods. Following USP compendial method for residual solvents as per supervisor.

RESULTS: Assay: 96.7% of declared USP specification: 90.0 – 105.0% of declared

Content Uniformity: At level 1 (n=10) Acceptance Value (AV) = 6.3
USP specification: AV ≤ L1 L1 = 15.0

NAI closed 2/19/07

Results continued on next page.

11. RESERVE SAMPLE

One whirl-pak bag officially sealed "377410 6-29-07 Susan L Young" and identified "377410 6-29-07 SLY" containing one intact bottle of product (sub 2) returned as received; one opened bottle of product (sub 1) further identified "SLY 4-10-07" containing 38 tablets; one glass bottle identified "Digoxin composite $\bar{x}$ 105.235mg 377410 4-11-07 SLY" containing ~ 2g of composite.

12. a. ANALYST SIGNATURE (Broke Seal ☒)	13. WORK-SHEET CHECK	a. BY
Susan L Young		
b. Virginia Stulz Dissolution		b. DATE: 7/5/07
c. Tina L Murphy	14. DATE REPORTED: 7/5/07	

Denver District Laboratory Electronic Form 431
2006 Version 1.0

Route to: NWJ DO

JRC AOCO 2/13/07

Non-Class 1

ATTACHMENT(S): A, B, C, D

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets USP 125µg	SAMPLE NUMBER 377410

7. Description of Sample continued

for lot # 70078A identified as "Sample # 377410 2/9/07 KAZ Attachment 3 page 1 of 1" and Amide Pharmaceutical, Inc methods of analysis identified "Sample # 37710 2/9/07 KAZ Attachment 4" and "page 1 of 16" through "page 16 of 16"

Results continued:

Dissolution: At Stage 1 (n=6) USP specification: Each unit not less than (Q+5)%. Q=80

Tablet	% Dissolution
1	106
2	98
3	104
4	99
5	106
6	103

Organic Volatile Impurities:

USP specification: "The amount of each organic volatile impurity present in the material does not exceed the limit given in the table shown below."

Organic Volatile Impurity	Limit (µg per g)
Chloroform	60
1,4-Dioxane	380
Methylene Chloride	600
Trichloroethylene	80

No organic volatile impurities detected. Sample meets specification.

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

Assay, Content Uniformity, Dissolution, Residual Solvents by USP (on-line official version 8/1/06 – 4/30/07) "Digoxin Tablets"

ASSAY
(USP specs: 90.0 – 105.0% of label)

Mobile Phase: 74 + 26 water + acetonitrile.

Diluent: 1 + 1 95% ethanol + water
(As per USP "Diluted Alcohol may be prepared as follows: Alcohol 500mL Purified Water 500mL")

Calibration Standard (CS): Dried in vacuum oven NC91167 4-11-07 1hr @ 105°C Balance: Mettler AT163 #NC90250 4-12-07

10.7 mg digoxin → 10.0mL with diluted alcohol
USP current lot OØBØ96 (0.961 mg/mg on the dried basis)

1.00mL above → 25.00mL with diluted alcohol (~ 40µg/mL)

Initial Calibration Verification (ICV):

~~11.0~~ 11.1 4-12-07 SCY mg digoxin → 10.0mL with diluted alcohol

1.00mL above → 25.00mL with diluted alcohol

System Suitability: Balance: Mettler AT 163 # NC90250 4-3-07

10.4 mg digoxigenin → 10.0mL with diluted alcohol

1.00mL above + 1.00mL stock ICV → 25.00mL with diluted alcohol

Continuing Calibration Verification (CCV): CS also used as CCV

Blank: diluted alcohol

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

ASSAY continued

Balance: Mettler AT163 # NC90250
4-11-07

Sample Composite Preparation:

Weight of 40 tablets to be finely ground 4.2094 g

Average tablet weight 105.235 mg

Sample prep:
(8 tablets x 125µg/tablet = 1mg)

842.7 mg composite to a 50mL conical tube.
Add 25.0mL diluted alcohol, swirl, sonicate 30min, cool.
Filter an aliquot of the supernatant discarding the first 10mL.

Duplicate: 852.7 mg composite to a 50mL conical tube.
Proceed as above.

High:
1.00mL stock CS → 20.00mL with diluted alcohol (~ 50µg/mL)

Lows:

① 1.00mL stock CS → 50.0mL with diluted alcohol (~ 20µg/mL)

② 1.00mL stock CS → 50.0mL with diluted alcohol (~ 20µg/mL)

③ 1.00mL stock CS → 50.0mL with diluted alcohol (~ 20µg/mL)

Matrix Spike:

0.5mL stock ICV + 409.5 mg composite → 25.0mL with diluted alcohol
(0.5mL x 1mg/mL = 0.5mg) (4 tablets x 125µg/tablet = 0.5mg)

ANALYST(S) Susan L Young

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

Assay, Content Uniformity, Dissolution, Residual Solvents
by USP "Digoxin Tabelts" on-line official version

HPLC System #5, FDA #1701616(computer) #1701614(DAD)
Column: Phenomenex Luna 5um 250x4.60mm SN 93923-29
System Suit: R (digoxigenin & digoxin) >= 4.0
RSD(5) <= 2.0%
TF (digoxin) <= 2.0
n (digoxin) <= 1200

System Suitability repetitive injections

Data file C:\HPCHEM\1\DATA\041207SY\

file ext	digoxigenin RT(min)	digoxigenin area	digoxin RT(min)	digoxin area
002-0202	5.192	1653.6	16.424	955.8
002-0203	5.189	1655.1	16.419	954.1
002-0204	5.189	1655.8	16.420	956.0
002-0205	5.186	1656.1	16.414	956.0
002-0206	5.187	1656.8	16.415	956.5

from data file 002-0206:	average	955.7
Resolution = 24.161	std dev	0.9
TF digoxin = 1.079	RSD	0.1
n digoxin = 8519		

Calculations w/ Excel 2003 (11.8117.8122) SP2

Calibration Standard

Data file C:\HPCHEM\1\DATA\041207SY\

file ext	digoxin RT(min)	digoxin area
003-0401	16.370	909.88556

Sample Injections

USP Specs: 90.0-105.0%

Data file C:\HPCHEM\1\DATA\041207SY\

file ext	digoxin RT(min)	digoxin area	ug digoxin per tablet	% of declared
005-0701	16.388	856.10645	120.8	96.7
006-0801	16.388	860.05627	120.0	96.0

Assay calc: std conc x spl dilution x avg tab wt x Au/As x 1000ug/mg = ug digoxin / tablet

005-0701: 10.7mg (0.961)/10.0mL x 1.00mL/25.0mL x 25.0mL/842.7mg x 105.235mg avg tab wt
x 856.10645/909.88556 x 1000ug/mg = 120.8ug / tablet

006-0801: 10.7mg (0.961)/10.0mL x 1.00mL/25.0mL x 25.0mL/852.7mg x 105.235mg avg tab wt
x 860.05627/909.88556 x 1000ug/mg = 120.0ug / tablet

Declared: 125ug/tablet USP specification: 90.0 - 105.0%

% difference sample & sample dup: (120.8 - 120.0) / [(120.8 + 120.0)] / 2 x 100 = 0.7% difference

ANALYST(S) Susan L Young

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GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

Quality Control

Calibration Standard (CS): 10.7mg (0.961)/10.0mL x 1.00mL/25mL = 41.1ug/mL
Response: 909.88556
Response/Conc: 909.88556/41.1 = 22.1

Initial Calibration Verification (ICV)

Data file C:\HPCHEM\1\DATA\041207SY\

file ext	digoxin RT(min)	digoxin area
004-0601	16.365	951.14551

ICV conc: 11.1mg (0.961)/10.0mL x 1.00mL/25.0mL = 42.7ug/mL
Response: 951.14551
Response/Conc: 951.14551/42.7 = 22.3
ICV Recovery: 22.3/22.1 x 100 = 100.9%

Continuing Calibration Verification (CCV)

Data file C:\HPCHEM\1\DATA\041207SY\

file ext	digoxin RT(min)	digoxin area
003-1501	16.356	924.38165
003-2101	16.389	916.10974

CCV conc: 41.1ug/mL
CCV1: response = 924.38165
Response/Conc: 924.38165/41.1 = 22.5
recovery = 22.5/22.1 x 100 = 101.8%
CCV2: Response: 916.10974
Response/Conc: 916.10974/41.1 = 22.3
recovery = 22.3/22.1 x 100 = 100.9%

Matrix Spike

Data file C:\HPCHEM\1\DATA\041207SY\

file ext	digoxin RT(min)	digoxin area
007-0901	16.381	903.54938

Total digoxin: 41.1ug/mL x 25.0mL x 903.54938/909.88556 = 1.020mg
Sample mg: 409.5mg/105.235mg/tab x 120.8mg digoxin/tab = 0.470mg
Difference: 1.020 - 0.470 = 0.550mg
Added: 11.1mg (0.961)/10.0mL x 0.5mL = 0.533mg
Matrix Spike Recovery: 0.550/0.533 x 100 = 103.2%

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

Quality Control continued

High

Data file C:\HPCHEM\1\DATA\041207SY\

file ext	digoxin RT(min)	digoxin area
021-2601	16.399	1172.62061

High conc: 10.7mg (0.961)/10.0mL x 1.00mL/20.0mL = 51.4ug/mL
Response: 1172.62061
Response/Conc: 1172.62061/51.4 = 22.8
High Recovery: 22.8/22.1 x 100 = 103.2%

Lows

Data file C:\HPCHEM\1\DATA\041207SY\

file ext	digoxin RT(min)	digoxin area
018-2301	16.399	468.14490
019-2401	16.405	462.41983
020-2501	16.410	461.31964

Low 1 (018-2301) conc: 10.7mg (0.961)/10.0mL x 1.00mL/50.0mL = 20.6ug/mL
Response: 468.14490
Response/Conc: 468.14490/20.6 = 22.7
Low 1 Recovery: 22.7/22.1 x 100 = 102.7%

Low 2 (019-2401) conc: 20.6ug/mL
Response: 462.41983
Response/Conc: 462.41983/20.6 = 22.4
Low 2 Recovery: 22.4/22.1 x 100 = 101.4%

average	101.8
std dev	0.75
RSD	0.7

Low 3 (020-2501) conc: 20.6ug/mL
Response: 461.31964
Response/Conc: 461.31964/20.6 = 22.4
Low 3 Recovery: 22.4/22.1 x 100 = 101.4%

ANALYST(S)

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

UNIFORMITY OF DOSAGE UNITS
(USP specs:
Level 1 (n=10): Acceptance Value (AV) = $|98.5 - \bar{x}| + 2.4(s)$
AV ≤ 15.0)

By Content Uniformity:

Individual Tablet Weights (mg) Balance: Mettler AE163 #NC90250 4-12-07

1)	109.0	6)	104.1
2)	104.4	7)	106.1
3)	102.7	8)	106.9
4)	103.8	9)	106.1
5)	106.4	10)	106.5

Each individual tablet in a 15mL conical tube.
Add 3.00mL diluted alcohol, swirl, sonicate 30min, cool.
Centrifuge and draw aliquot from the supernatant.

Sorvall RT 6000D
#1701413
4-12-07

ANALYST(S) Susan E Young

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GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

UNIFORMITY OF DOSAGE UNITS

Content Uniformity level 1
Data file C:\HPCHEM\1\DATA\041207SY\

	file ext	digoxin RT(min)	digoxin area	ug digoxin per tablet	% of declared	
tablet 1	008-1001	16.389	890.91492	120.8	96.7	
tablet 2	009-1101	16.394	862.61694	117.0	93.6	
tablet 3	010-1201	16.386	880.40179	119.4	95.5	
tablet 4	011-1301	16.384	881.50073	119.5	95.6	
tablet 5	012-1401	16.380	892.34027	121.0	96.8	
tablet 6	013-1601	16.381	887.99988	120.4	96.3	avg % of
tablet 7	014-1701	16.389	890.26398	120.7	96.6	declared
tablet 8	015-1801	16.392	928.09546	125.9	100.7	96.8
tablet 9	016-1901	16.402	907.32068	123.0	98.4	std dev
tablet 10	017-2001	16.410	897.28046	121.7	97.3	1.9

mg digoxin/tablet = std conc x smpl dilution x Au/As x 1000ug/mg

representative calc using tablet #1:

10.7mg (0.961)/10.0mL x 1.00mL/25.0mL x 3mL
x 890.91492/909.88556 x 1000ug/mg = 120.82ug

% of declared = 120.82/125 x 100 = 96.7%

USP Acceptance Value (AV) = I 98.5 - $\bar{x}$ I + 2.4s

AV = (98.5 - 96.8) + (2.4)(1.9) = 6.3

At n = 10, requirements are met if AV <= L1. L1 = 15.0

ANALYST(S)

FORM FDA 431a (2006) Version 1.0

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

"<467> Organic Volatile Impurities (Current title – not to change until July 1, 2007)"

Method I

Balance: Mettler AE163 #NC90250
6-12-07 SLY

Stock Standard:
(Each mL to contain ~ 4800µg methylene chloride
3040µg 1,4-dioxane
640µg trichloroethylene
480µg chloroform)

113.9 mg methylene chloride + 75.9 mg 1,4-dioxane +
15.4 mg trichloroethylene + 11.6 mg chloroform → 25.0mL with water

Working Standard ①:
(Each mL to contain ~ 600µg methylene chloride
380µg 1,4-dioxane
80µg trichloroethylene
60µg chloroform)

1.00mL stock standard + 7.00mL water

Working Standard ②:
(Each mL to contain ~ 480µg methylene chloride
304µg 1,4-dioxane
64µg trichloroethylene
48µg chloroform

1.00mL stock standard + 9.00mL water

Sample Prep:
(~ 20mg/mL)

213.8 mg sample → 10.0mL with water

Matrix Spikes:

① 0.50mL sample (383390) + 0.5mL stock standard

② 1.00mL sample (383391) + 0.5mL stock standard

Blank: water

Sample meets the specifications below.

USP Specs: The amt of ea OVI present does not exceed the limits of WS① above.

ANALYST(S) Susan C Young	PAGE 10 OF 15 PAGES

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GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

Organic Volatile Impurities

Compound	WS 1	WS 2	Blank	377410	408376	414717	420529	412621	420501
Methylene Chloride	+	+	-	-	-	-	-	-	-
Chloroform	+	+	-	-	-	-	-	-	-
Trichloroethylene	+	+	-	-	-	-	-	-	-
1,4-dioxane	+	+	-	-	-	-	-	-	-

Compound	383890	383890 spike	383891	383891 spike	408372	409673	409674	423339
Methylene Chloride	-	+	-	+	-	-	-	-
Chloroform	-	+	-	+	-	-	-	-
Trichloroethylene	-	+	-	+	-	-	-	-
1.4-dioxane	-	+	-	+	-	-	-	-

Compound	423340	396200	420503					
Methylene Chloride	-	-	-					
Chloroform	-	-	-					
Trichloroethylene	-	-	-					
1.4-dioxane	-	-	-					

"+" indicates that the spectrum matched the Wiley Library search for that compound.
"-" indicates that there was no match.

ANALYST(S) Susan L Young

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

DISSOLUTION
(USP specs:
S1: Each unit not less than Q + 5%. (Q = 80%) (Number tested = 6)
S2: Average of 12 units (S1 + S2) ≥ Q & no unit < Q – 5 (Number tested = 6))

Glassware Rinse:
① Dilute HCl
② Water
③ Alcohol
④ Dry

Balance: Mettler AE-163 #WC902250 6-27-07 SCY

Ascorbic acid – methanol solution: 2mg ascorbic acid/mL methanol
40.6mg → 20.0mL

Standard Solutions:

① 25.1 mg digoxin + minimum alcohol to dissolve → 500.0mL with dilute alcohol
(~ 0.050mg/mL) (As per USP: "dilute alcohol (4 in 5)")

② 10.0mL above → 100.0mL with dilute alcohol (~ 5000ng/mL)

JUST PRIOR TO USE
20% – 100% 5-point curve of labeled amount of digoxin in 500mL (125µg/500mL = 250ng/mL)

% solution	mL soln of ② above	Q.S. w 0.1N HCl	Concentration
20	0.500	50.0	50 ng/mL
40	1.00	50.0	100 ng/mL
60	3.00	100.0	150 ng/mL
80	2.00	50.0	200 ng/mL
100	5.00	100.0	250 ng/mL

ON DAY OF USE – Hydrogen peroxide – methanol solution:
2.0mL 30% H_2O_2 → 100mL with methanol
STORE IN REFRIGERATOR
JUST PRIOR TO USE – 2.0mL above → 100mL with methanol

ANALYST(S) Susan L Young

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

DISSOLUTION continued

Instrument: Vankel Dissolution Apparatus #1 FDA # 1700667
Apparatus 1 – baskets: 100rpm
Medium: 500mL 0.1N HCl
Time: 60 minutes
Temperature: 37 ± 0.5°
Thermometer: Fluke 52 K/J, FDA #NC91257

Sample solutions:
Filter aliquot through a 0.8µm or finer filter, discarding the first ten mL.

Procedure:
Transfer to individual 25mL glass stoppered erlenmeyers duplicate 1.0mL portions of:
Blank (0.1N HCl dissolution medium)
Standard solutions (50 → 250 ng/mL)
Sample solutions

Treating one flask at a time, quickly add in the named order:
1.0mL ascorbic acid – methanol solution
5.0mL HCl
1.0mL hydrogen peroxide – methanol solution

Insert stopper, wait 2 hours.
Measure the fluorescence at ~ 485nm with excitation λ ~ 372nm.
Use one or more standard solutions as CCVs (continuous calibration verification).
Correct each reading for the blank.

Note: 4 tablets used for various preliminary tests + observations.

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

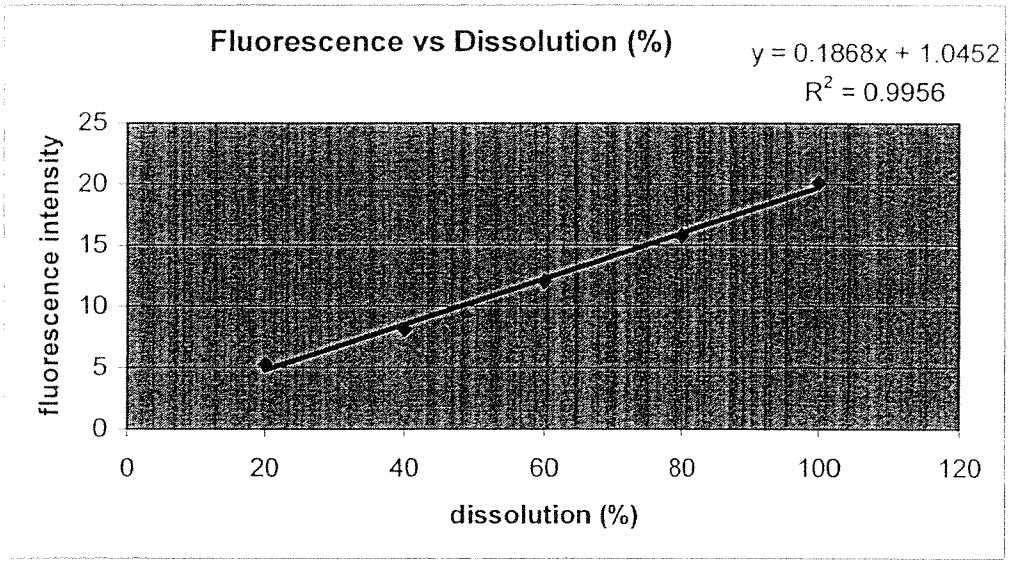
Dissolution measured by fluorescence with excitation at 372nm & emission at 485nm

P-E LS50 Luminescence Spectrometer
Serial#3057 FDA#1701410

As per USP:
Duplicate portions of each solution are read.
To check the stability of the fluorometer, the measurement of fluorescence is repeated on one or more treated standards.
Each reading is corrected for the blank.

I/M 6/27/07

dissolution	fluorescence	avg	(%) dissolution	avg minus blank
blank a	0.945			
blank b	0.881	0.913		
20a	7.123			
20b	5.199	6.161	20	5.248
40a	8.788			
40b	9.253	9.0205	40	8.108
60a	12.966			
60b	12.934	12.950	60	12.037
80a	16.935			
80b	16.418	16.6765	80	15.764
100a	20.851			
100b	21.165	21.008	100	20.095



Excel 2003(11.8134.8132)SP2

ANALYST(S)
Susan L Young

FORM FDA 431a (2006) Version 1.0

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets, USP 125µg	SAMPLE NUMBER 377410

x = (y -1.0452) / 0.1868

dissolution	fluorescence	avg	avg-blank	dissolution(%)
tablet 1a	21.685			
tablet 1b	21.694	21.6895	20.7765	106
tablet 2a	20.029			
tablet 2b	20.460	20.2445	19.3315	98
tablet 3a	21.755			
tablet 3b	21.056	21.4055	20.4925	104
tablet 4a	20.627			
tablet 4b	20.344	20.486	19.5725	99
tablet 5a	22.756			
tablet 5b	20.723	21.7395	20.8265	106
tablet 6a	20.873			
tablet 6b	21.442	21.158	20.2445	103

		- blank	(%) dissolution	recovery(%)
CCV 60a	12.828	11.915	58	97
CCV 60b	12.770	11.857	58	97

USP Specs S1:
Each unit not less than
(Q+5)% (Q=80) # tested = 6.

ANALYST(S) Susan L Young

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FORM FDA 431a (2006) Version 1.0

377410
5-3-07
SLY

Attachment A

Assay & Content Uniformity
Chromatography

Sequence: C:\HPCHEM\1\SEQUENCE\DIGOXIN.S

Sample # 377410
Attachment A pg 1 of 44
SLY 5-3-07

Sequence Table:

Method and Injection Info Part:

Line	Vial	SampleName	Method	Inj	SampleType	InjVolume	DataFile
1	1	blank	DIGOXIN	1	Sample		
2	2	system suit	DIGOXIN	6	Sample		
3	1	blank	DIGOXIN	1	Sample		
4	3	CS	DIGOXIN	1	Sample		
5	1	blank	DIGOXIN	1	Sample		
6	4	ICV	DIGOXIN	1	Sample		
7	5	377410assay1	DIGOXIN	1	Sample		
8	6	377410assay2	DIGOXIN	1	Sample		
9	7	matrix spike	DIGOXIN	1	Sample		
10	8	CU1	DIGOXIN	1	Sample		
11	9	CU2	DIGOXIN	1	Sample		
12	10	CU3	DIGOXIN	1	Sample		
13	11	CU4	DIGOXIN	1	Sample		
14	12	CU5	DIGOXIN	1	Sample		
15	3	CCV	DIGOXIN	1	Sample		
16	13	CU6	DIGOXIN	1	Sample		
17	14	CU7	DIGOXIN	1	Sample		
18	15	CU8	DIGOXIN	1	Sample		
19	16	CU9	DIGOXIN	1	Sample		
20	17	CU10	DIGOXIN	1	Sample		
21	3	CCV	DIGOXIN	1	Sample		
22	1	blank	DIGOXIN	1	Sample		
23	18	MDL1	DIGOXIN	1	Sample		
24	19	MDL2	DIGOXIN	1	Sample		
25	20	MDL3	DIGOXIN	1	Sample		
26	21	high	DIGOXIN	1	Sample		
27	none	flush	FLUSH	1	Sample		

Computer
HPLC #5 FDA# 17016616

Dad17016614

4-12-07

Method: C:\HPCHEM\1\METHODS\DIGOXIN.M of 4/13/07 12:33:20 PM

Sample # 377410
Attachment A pg 2 of 44
SLY
5-3-07

Method Information

digoxin

Run Time Checklist

Pre-Run Cmd/Macro:	off
Data Acquisition:	on
Standard Data Analysis:	on
Customized Data Analysis:	off
Save GLP Data:	off
Post-Run Cmd/Macro:	off
Save Method with Data:	skipped - no ACQ running

Method: C:\HPCHEM\1\METHODS\DIGOXIN.M of 4/13/07 12:33:20 PM

Sample # 37740
Attachment A pg 3 of 44
SLY 5-3-07

HP 1100 Quaternary Pump 1

Control

Flow	:	1.250 ml/min
Stoptime	:	20.00 min
Posttime	:	Off

Solvents

Solvent A	:	50.0 % (mobile phase)
Solvent B	:	50.0 % (mobile phase)
Solvent C	:	0.0 % (65% ACN)
Solvent D	:	0.0 % (50% ACN)

PressureLimits

Minimum Pressure	:	0 bar
Maximum Pressure	:	220 bar

Auxiliary

Maximal Flow Ramp	:	100.00 ml/min^2
Primary Channel	:	Auto
Compressibility	:	100*10^-6/bar
Minimal Stroke	:	Auto

Store Parameters

Store Ratio A	:	Yes
Store Ratio B	:	Yes
Store Ratio C	:	Yes
Store Ratio D	:	Yes
Store Flow	:	Yes
Store Pressure	:	Yes

HP 1100 Contacts Option

Contact 1	:	Open
Contact 2	:	Open
Contact 3	:	Open
Contact 4	:	Open

HP 1100 Diode Array Detector 1

Method: C:\HPCHEM\1\METHODS\DIGOXIN.M of 4/13/07 12:33:20 PM

Signals

Signal	Store	Signal,Bw		Reference,Bw		[nm]
A:	Yes	218	4	350	40	
B:	No	254	4	360	25	
C:	No	220	4	360	50	
D:	No	230	16	360	100	
E:	No	280	4	350	20	

Sample # 377410
Attachment A pg 4 of 44
SLY
5-3-07

Spectrum
Store Spectra : None

Time
Stoptime : As pump
Posttime : Off

Required Lamps
UV lamp required : Yes
Vis lamp required : Yes

Autobalance
Prerun balancing : Yes
Postrun balancing : No
Margin for negative Absorbance: 100 mAU

Peakwidth : > 0.1 min
Slit : 4 nm

Analog Outputs
Zero offset ana. out. 1: 5 %
Zero offset ana. out. 2: 5 %
Attenuation ana. out. 1: 1000 mAU
Attenuation ana. out. 2: 1000 mAU

HP 1100 Contacts Option
==========

Contact 1 : Open
Contact 2 : Open
Contact 3 : Open
Contact 4 : Open

==========
HP 1100 Autosampler 1
==========

Method: C:\HPCHEM\1\METHODS\DIGOXIN.M of 4/13/07 12:33:20 PM

Injection

Injection Mode	:	Standard
Injector volume	:	25.0 µl

Sample # 377419
Attachment A pg 5 of 44
SLY 5-3-07

Auxiliary

Drawspeed	:	200 µl/min
Ejectspeed	:	200 µl/min
Draw position	:	0.0 mm

Time

Stoptime	:	As Pump
Posttime	:	Off

==========

HP 1100 Column Thermostat 1

==========

Temperature settings

Left temperature	:	20.0°C
Right temperature	:	Same as left
Enable analysis	:	When Temp. is within setpoint +/- 0.5°C
Store left temperature	:	Yes
Store right temperature	:	No

Time

Stoptime	:	As pump
Posttime	:	Off

Column Switching Valve : Column 1

==========

Integration Events

==========

Results will be produced with the enhanced integrator.

Default Integration Event Table "Event"

Event	Value	Time
Initial Slope Sensitivity	1.000	Initial
Initial Peak Width	0.040	Initial
Initial Area Reject	1.000	Initial
Initial Height Reject	1.700	Initial
Initial Shoulders	OFF	Initial

Method: C:\HPCHEM\1\METHODS\DIGOXIN.M of 4/13/07 12:33:20 PM

Detector Default Integration Event Table "Event_ADC"

Event	Value	Time
Initial Slope Sensitivity	1.000	Initial
Initial Peak Width	0.040	Initial
Initial Area Reject	1.000	Initial
Initial Height Reject	1.700	Initial
Initial Shoulders	OFF	Initial

Sample # 377410 Attachment A pg 6 of 44 SLY 5-3-07

Detector Default Integration Event Table "Event_FLD"

Event	Value	Time
Initial Slope Sensitivity	1.000	Initial
Initial Peak Width	0.040	Initial
Initial Area Reject	1.000	Initial
Initial Height Reject	1.700	Initial
Initial Shoulders	OFF	Initial

Detector Default Integration Event Table "Event_VWD"

Event	Value	Time
Initial Slope Sensitivity	1.000	Initial
Initial Peak Width	0.040	Initial
Initial Area Reject	1.000	Initial
Initial Height Reject	1.700	Initial
Initial Shoulders	OFF	Initial

Detector Default Integration Event Table "Event_ECD"

Event	Value	Time
Initial Slope Sensitivity	1.000	Initial
Initial Peak Width	0.040	Initial
Initial Area Reject	1.000	Initial
Initial Height Reject	1.700	Initial
Initial Shoulders	OFF	Initial

Method: C:\HPCHEM\1\METHODS\DIGOXIN.M of 4/13/07 12:33:20 PM

Detector Default Integration Event Table "Event_MWD"

Sample # 372410
Attachment A pg 7 of 44
SLY 5-3-07

Event	Value	Time
Initial Slope Sensitivity	1.000	Initial
Initial Peak Width	0.100	Initial
Initial Area Reject	1.000	Initial
Initial Height Reject	0.500	Initial
Initial Shoulders	OFF	Initial
Integration OFF		0.000
Integration ON		2.000

Detector Default Integration Event Table "Event_DAD"

Event	Value	Time
Initial Slope Sensitivity	1.000	Initial
Initial Peak Width	0.300	Initial
Initial Area Reject	10.000	Initial
Initial Height Reject	3.000	Initial
Initial Shoulders	OFF	Initial
Integration OFF		0.000
Integration ON		4.000

Apply Manual Integration Events: No

Calibration Table

Calib. Data Modified : 4/12/07 2:07:40 PM

Calculate : Area Percent

Rel. Reference Window : 5.000 %
Abs. Reference Window : 0.000 min
Rel. Non-ref. Window : 5.000 %
Abs. Non-ref. Window : 0.000 min
Uncalibrated Peaks : not reported
Partial Calibration : Yes, identified peaks are recalibrated
Correct All Ret. Times: No, only for identified peaks

Method: C:\HPCHEM\1\METHODS\DIGOXIN.M of 4/13/07 12:33:20 PM

Curve Type : Linear
Origin : Included
Weight : Equal

Sample # 377470
Attachment A pg 8 of 44
SLY
5-3-07

Recalibration Settings:
Average Response : Average all calibrations
Average Retention Time: Floating Average New 75%

Calibration Report Options :
Printout of recalibrations within a sequence:
Calibration Table after Recalibration
Normal Report after Recalibration
If the sequence is done with bracketing:
Results of first cycle (ending previous bracket)

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

RetTime [min]	Lvl Sig		Amount [ng/ul]	Area	Amt/Area	Ref	Grp	Name
5.187	1	1	1.00000	1321.81433	7.56536e-4			digoxigenin
16.352	1	1	1.00000	760.22760	1.31540e-3			digoxin

Peak Sum Table

No Entries in table

Extended Performance Report

Sample # 377410
Attachment SLY A pg 9 of 44
5-3-07

Instrument: Instrument 5

Module	Firmware revision	Serial number
HP 1100 Autosampler	A.01.05	US54000690
HP 1100 Diode Array Detector	A.01.04	US61800254
HP 1100 Quaternary Pump	A.01.06	US53601017
HP 1100 Column Thermostat	A.01.06	US54001050

Software Revision: Rev. A.06.03 [509]

Analysis method: C:\HPCHEM\1\METHODS\DIGOXIN.M

Sample information for vial#: 2

Sample Name: system suit
Injection#: 6
Injection volume: 25 µl
Multiplier: 1.00
Dilution: 1.00

Acquisition information:

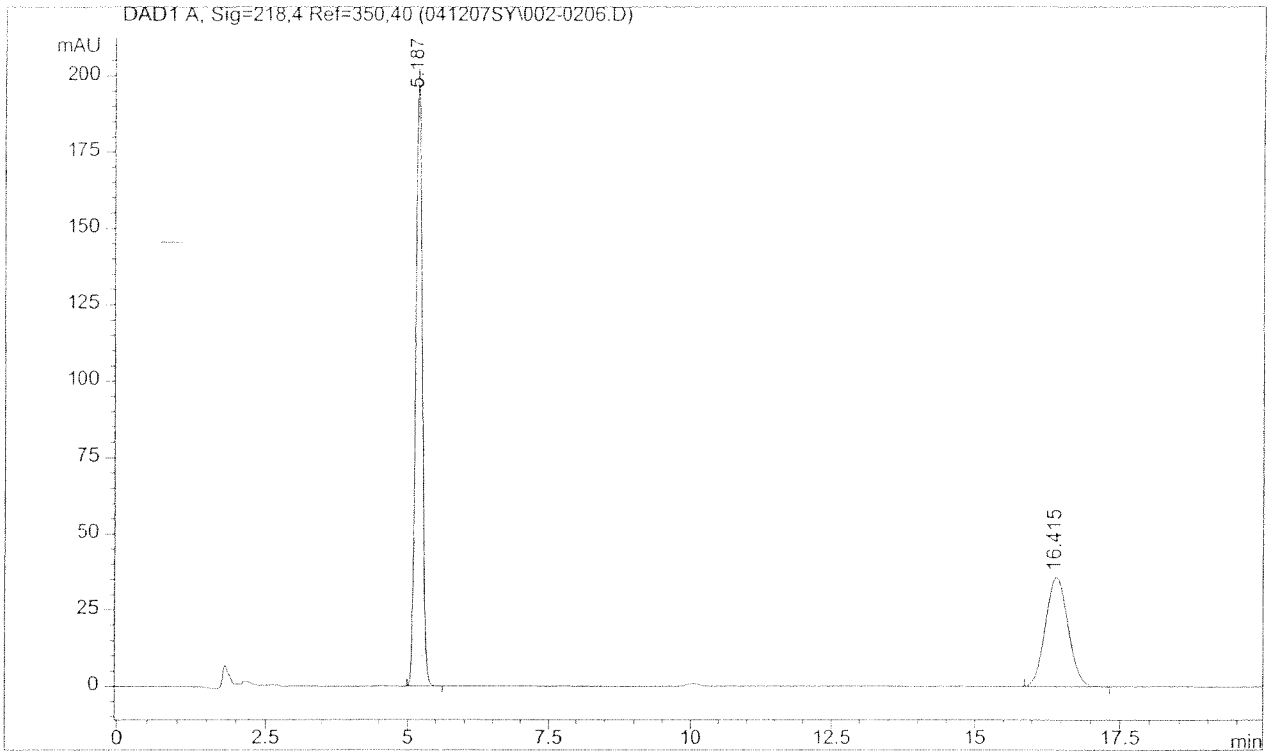
Operator: sly
Date/Time: 12-Apr-07, 16:55:18
Data file name: C:\HPCHEM\1\DATA\041207SY\002-0206.D
Method file name:

Flow: 1.250 ml/min
Pressure at start: 168 bar
Temperature at start: - °C
Pressure at end: 169 bar
Temperature at end: - °C

Solvents: PMP1, Solvent Amobile phase
PMP1, Solvent Bmobile phase
PMP1, Solvent C65% ACN
PMP1, Solvent D50% ACN

Signal description: DAD1 A, Sig=218,4 Ref=350,40

Data File C:\HPCHEM\1\DATA\041207SY\002-0206.D Sample Name: system suit



Sample # 377419
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SLY
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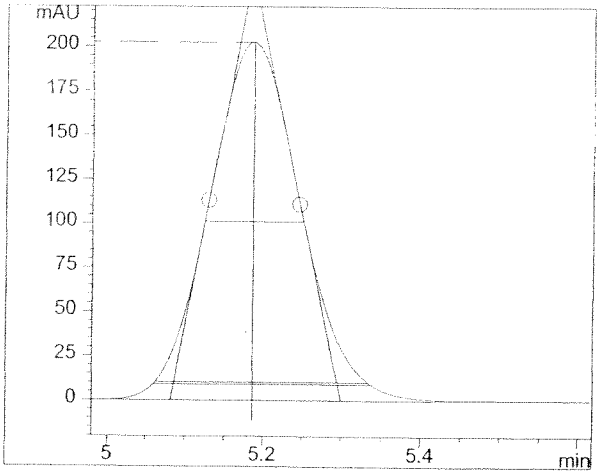
Data File C:\HPCHEM\1\DATA\041207SY\002-0206.D Sample Name: system suit

Compound# 1 : digoxigenin
Amount [ng/ul]: 1.2534

Sample # 377410
Attachment A Pg 11 of 44
SLY 5-3-07

Peak description [min]:
Signal: DAD1 A, Sig=218,4 Ref=350,40

RetTime:	5.187	k':	-
Height:	202.45	Area:	1656.8
Start:	4.985	End:	5.612
Skew:	0.374	Excess:	0.738
Width at half height:			0.125
5 sigma:			0.277
tangent:			0.218
tailing:			0.270
Symmetry:			0.891
USP Tailing:			1.099
Integration type:			BB
Time increment [msec]:			400.0
Data points:			105



Statistical moments (BB peak detection):

M0:	1655.5		
M1:	5.189	Tangent method	9048
M2:	0.003181	Halfwidth method	9538
M3:	0.000067	5 sigma method	8786
M4:	0.000038	Statistical	8464

Efficiency: Plates per ..

	column	meter
Tangent method	9048	-
Halfwidth method	9538	-
5 sigma method	8786	-
Statistical	8464	-

Relationship to preceeding peak:

Resolution	Tangent method:	-	Selectivity: -
	Halfwidth method	-	5 sigma method -
			Statistical method -

Data File C:\HPCHEM\1\DATA\041207SY\002-0206.D Sample Name: system suit

Compound# 2 : digoxin
Amount [ng/ul]: 1.2581

Sample # 37410
Attachment A pg 12 of 44
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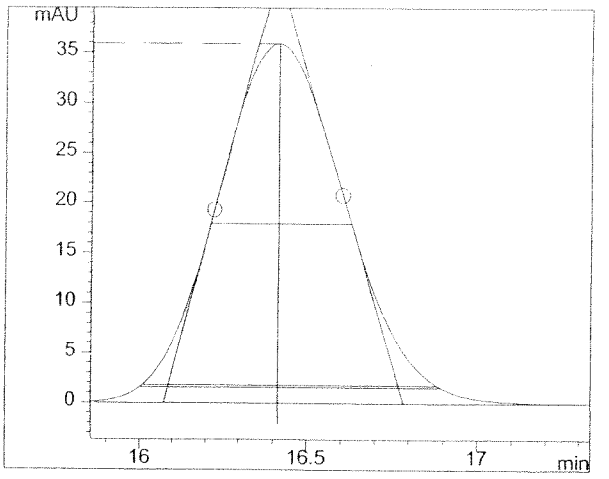
Peak description [min]:
Signal: DAD1 A, Sig=218,4 Ref=350,40

RetTime:	16.415	k':	-
Height:	35.91	Area:	956.5
Start:	15.865	End:	17.319
Skew:	0.224	Excess:	0.118
Width at half height:			0.413
5 sigma:			0.890
tangent:			0.711
tailing:			0.870
Symmetry:			0.899
USP Tailing:			1.079
Integration type:			BB
Time increment [msec]:			400.0
Data points:			313



Statistical moments (BB peak detection):

			Efficiency: Plates per ..	
			column	meter
M0:	949.4			
M1:	16.428	Tangent method	8519	-
M2:	0.031595	Halfwidth method	8738	-
M3:	0.001258	5 sigma method	8505	-
M4:	0.003112	Statistical	8542	-

Relationship to preceeding peak:

Resolution Tangent method:	24.161	Selectivity:	3.165
Halfwidth method	24.508	5 sigma method	24.061
		Statistical method	24.001

Data File C:\HPCHEM\1\DATA\041207SY\002-0206.D Sample Name: system suit

#	Ret.Time [min]	Amount [ng/ul]	Name	Page #
1	5.187	1.2534	digoxigenin	3
2	16.415	1.2581	digoxin	4
	Total:	2.5116		

*** End of Report ***

Sample # 377410
Attachment A pg 13 of 44
SLY
5-3-07

Data File C:\HPCHEM\1\DATA\041207SY\001-0101.D Sample Name: blank

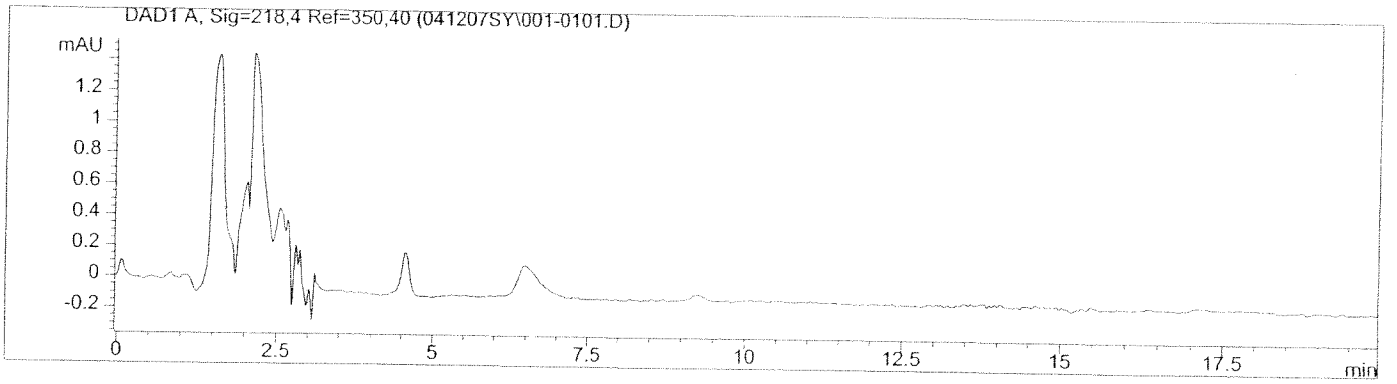
Injection Date : 4/12/07 2:46:46 PM
Sample Name : blank
Acq. Operator : sly

Seq. Line : 1
Vial : 1
Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 327410
Attachment A pg 14 of 44
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.352		0.0000	0.00000	0.0000	digoxin

Totals : 0.00000

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Instrument 5 4/13/07 12:49:02 PM sly

Data File C:\HPCHEM\1\DATA\041207SY\002-0201.D Sample Name: system suit

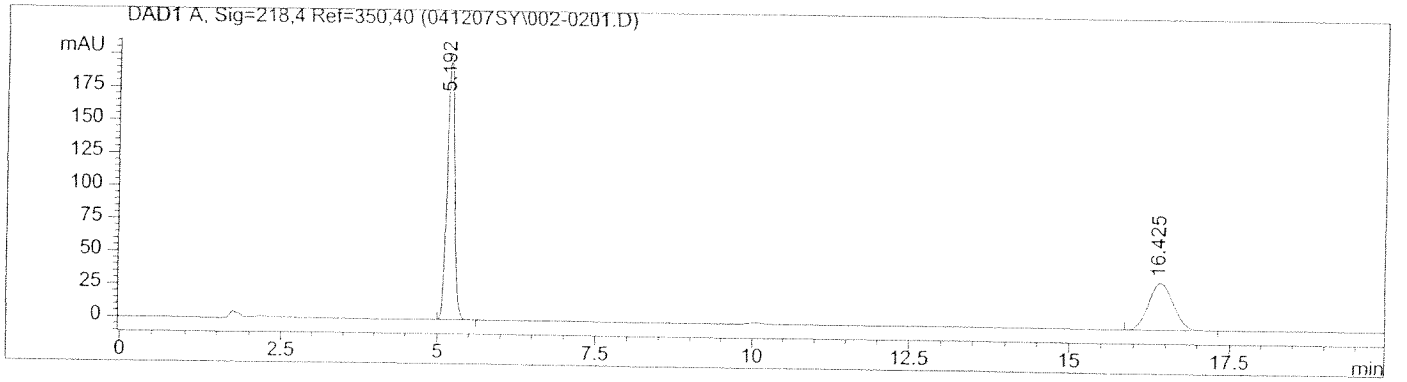
Injection Date : 4/12/07 3:08:12 PM
Sample Name : system suit
Acq. Operator : sly

Seq. Line : 2
Vial : 2
Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
Attachment A pg 15 of 44
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.192	BB	0.1281	1655.05432	63.4191	digoxigenin
2	16.425	BB	0.4207	954.65436	36.5809	digoxin

Totals : 2609.70868

Results obtained with enhanced integrator!

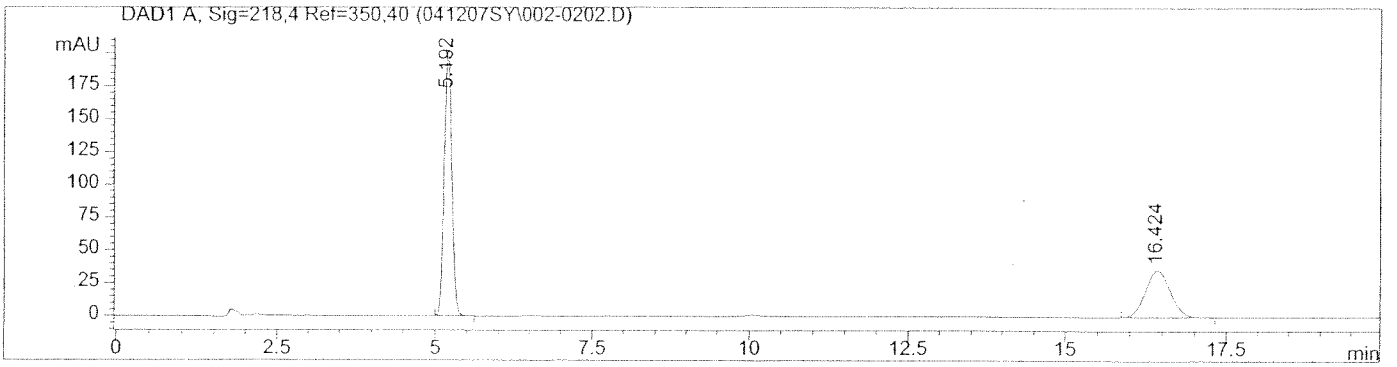
*** End of Report ***

Data File C:\HPCHEM\1\DATA\041207SY\002-0202.D Sample Name: system suit

Injection Date	: 4/12/07 3:29:36 PM	Seq. Line	: 2
Sample Name	: system suit	Vial	: 2
Acq. Operator	: sly	Inj	: 2
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410
Attachment A pg 16 of 44
SLY
5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.192	BB	0.1277	1653.57605	63.3702	digoxigenin
2	16.424	BB	0.4206	955.81311	36.6298	digoxin

Totals : 2609.38916

Results obtained with enhanced integrator!

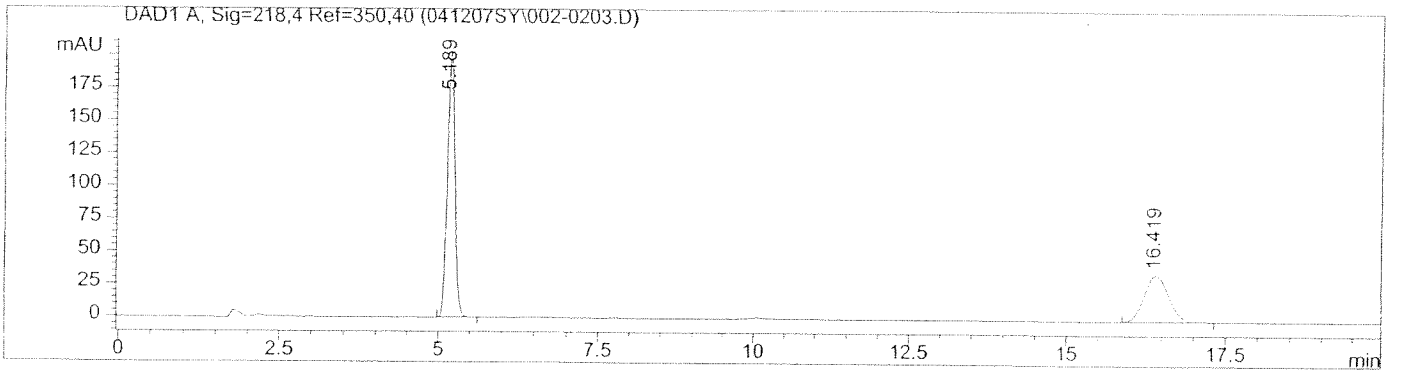
*** End of Report ***

Data File C:\HPCHEM\1\DATA\041207SY\002-0203.D Sample Name: system suit

Injection Date	: 4/12/07 3:51:01 PM	Seq. Line	: 2
Sample Name	: system suit	Vial	: 2
Acq. Operator	: sly	Inj	: 3
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410 Attachment A pg 17 of 44 SLY 5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.189	BB	0.1316	1655.14294	63.4337	digoxigenin
2	16.419	BB	0.4153	954.10608	36.5663	digoxin

Totals : 2609.24902

Results obtained with enhanced integrator!

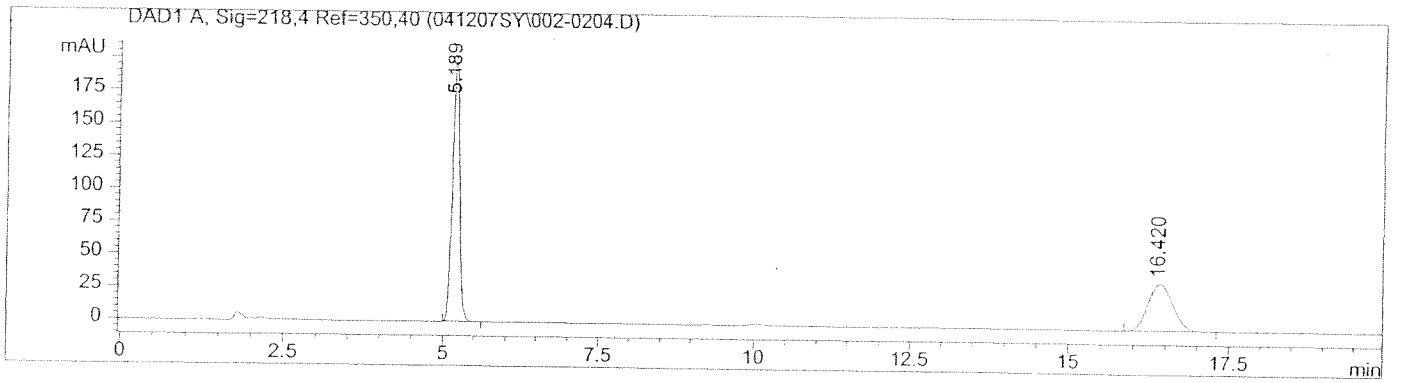
*** End of Report ***

Data File C:\HPCHEM\1\DATA\041207SY\002-0204.D Sample Name: system suit

Injection Date	: 4/12/07 4:12:27 PM	Seq. Line	: 2
Sample Name	: system suit	Vial	: 2
Acq. Operator	: sly	Inj	: 4
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410
Attachment A pg 18 of 44
SLY
5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.189	BB	0.1315	1655.77051	63.3959	digoxigenin
2	16.420	BB	0.4152	956.02515	36.6041	digoxin

Totals : 2611.79565

Results obtained with enhanced integrator!

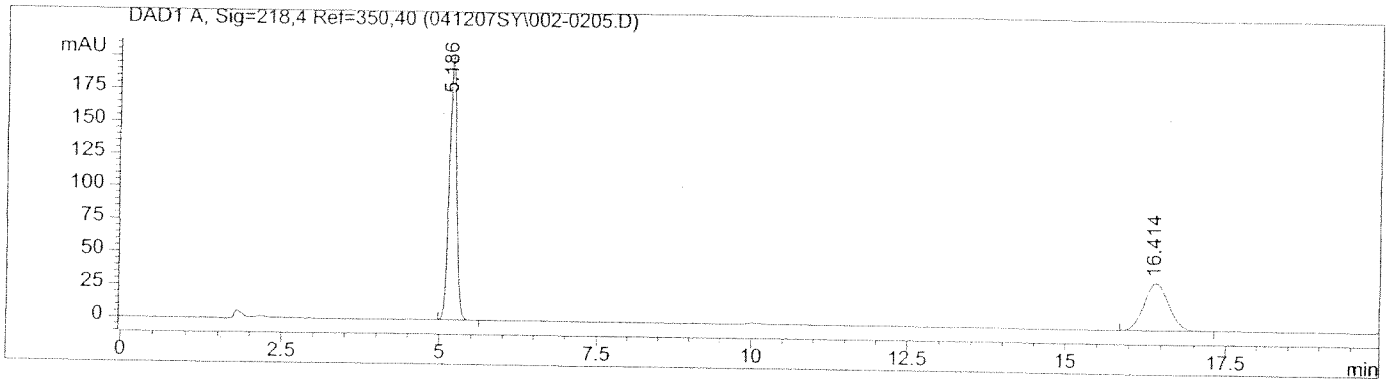
*** End of Report ***

Data File C:\HPCHEM\1\DATA\041207SY\002-0205.D Sample Name: system suit

Injection Date	: 4/12/07 4:33:52 PM	Seq. Line :	2
Sample Name	: system suit	Vial :	2
Acq. Operator	: sly	Inj :	5
		Inj Volume :	25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410 Attachment A pg 19 of 44 SLY 5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.186	BB	0.1315	1656.08374	63.4009	digoxigenin
2	16.414	BB	0.4189	955.99823	36.5991	digoxin
Totals :				2612.08197		

Results obtained with enhanced integrator!

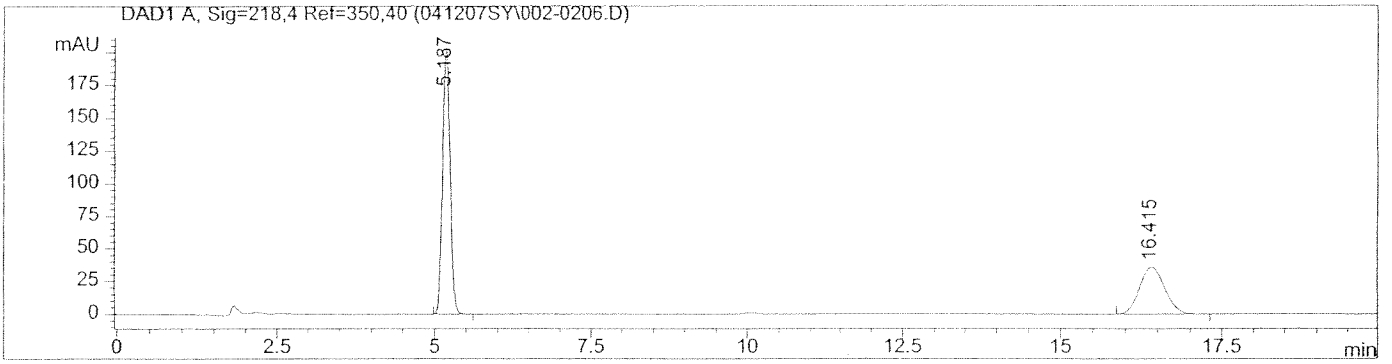
*** End of Report ***

Data File C:\HPCHEM\1\DATA\041207SY\002-0206.D Sample Name: system suit

Injection Date	: 4/12/07 4:55:18 PM	Seq. Line	: 2
Sample Name	: system suit	Vial	: 2
Acq. Operator	: sly	Inj	: 6
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410 Attachment A pg 20 of 44 SLY 5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187	BB	0.1315	1656.81995	63.4001	digoxigenin
2	16.415	BB	0.4147	956.45477	36.5999	digoxin

Totals : 2613.27472

Results obtained with enhanced integrator!

*** End of Report ***

Data File C:\HPCHEM\1\DATA\041207SY\001-0301.D Sample Name: blank

Injection Date : 4/12/07 5:16:45 PM Seq. Line : 3
Sample Name : blank Vial : 1
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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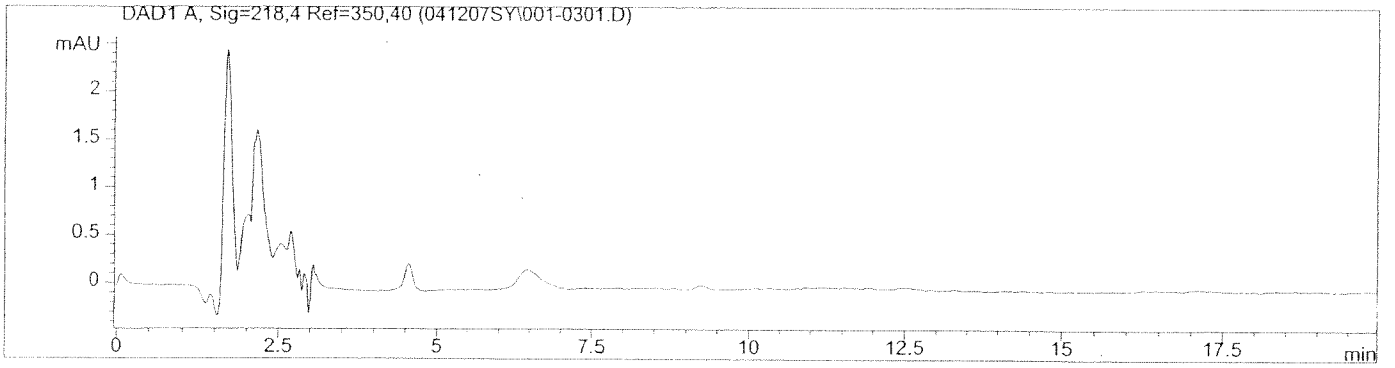
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.352		0.0000	0.00000	0.0000	digoxin

Totals : 0.00000

Results obtained with enhanced integrator!
1 Warnings or Errors :

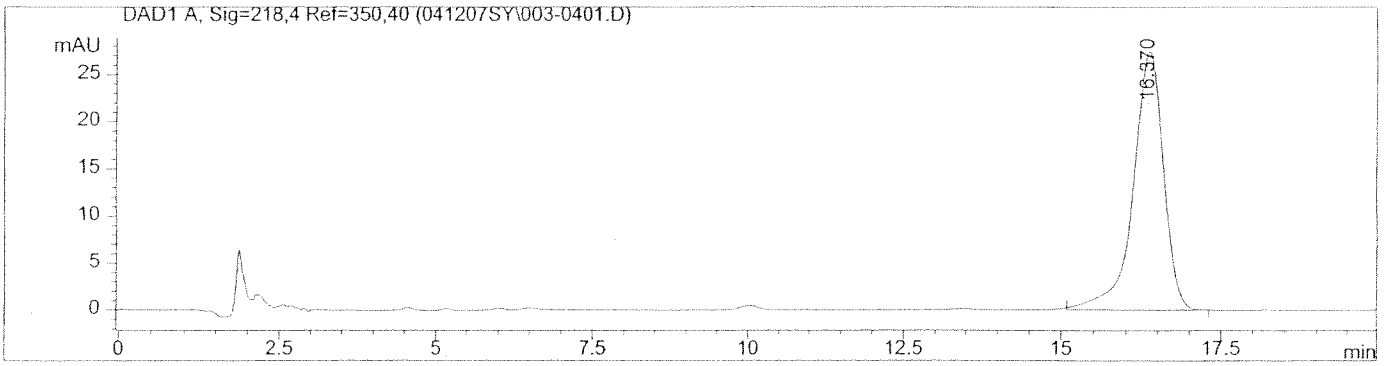
Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\003-0401.D Sample Name: CS

Injection Date	: 4/12/07 5:38:11 PM	Seq. Line	: 4
Sample Name	: CS	Vial	: 3
Acq. Operator	: sly	Inj	: 1
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 37740 Attachment A pg 22 of 44 SLY 5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.370	BB	0.5025	909.88556	100.0000	digoxin

Totals : 909.88556

Results obtained with enhanced integrator!
1 Warnings or Errors :

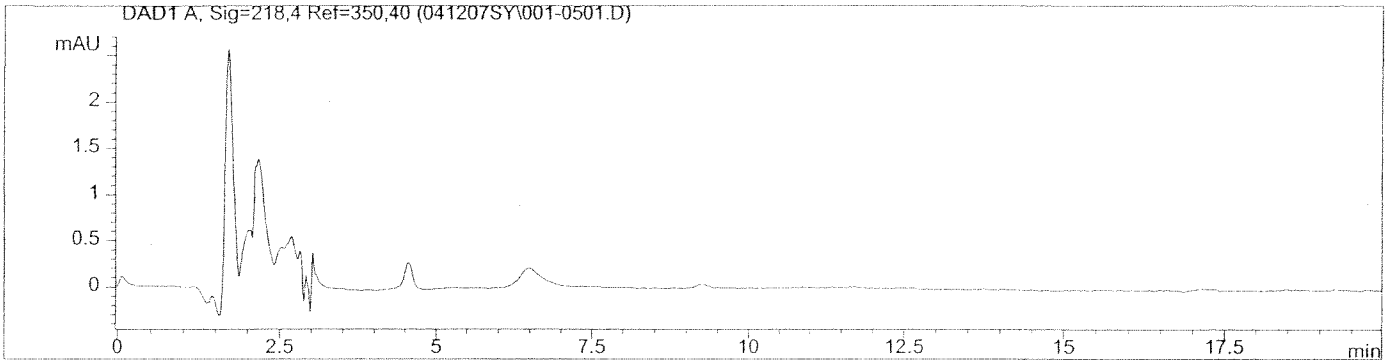
Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\001-0501.D Sample Name: blank

Injection Date	: 4/12/07 5:59:37 PM	Seq. Line	: 5
Sample Name	: blank	Vial	: 1
Acq. Operator	: sly	Inj	: 1
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly		
	(modified after loading)		

Sample # 377410 Attachment A pg 23 of 44 SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.352		0.0000	0.00000	0.0000	digoxin

Totals : 0.00000

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\004-0601.D Sample Name: ICV

Injection Date : 4/12/07 6:21:05 PM Seq. Line : 6
Sample Name : ICV Vial : 4
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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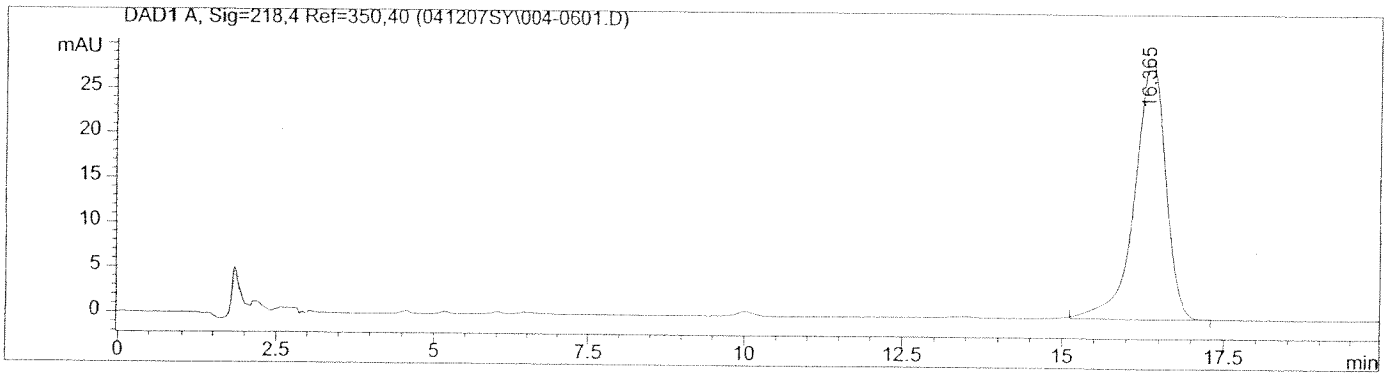
digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.365	BB	0.4987	951.14551	100.0000	digoxin

Totals : 951.14551

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\005-0701.D Sample Name: 377410assay1

Injection Date : 4/12/07 6:42:32 PM Seq. Line : 7
Sample Name : 377410assay1 Vial : 5
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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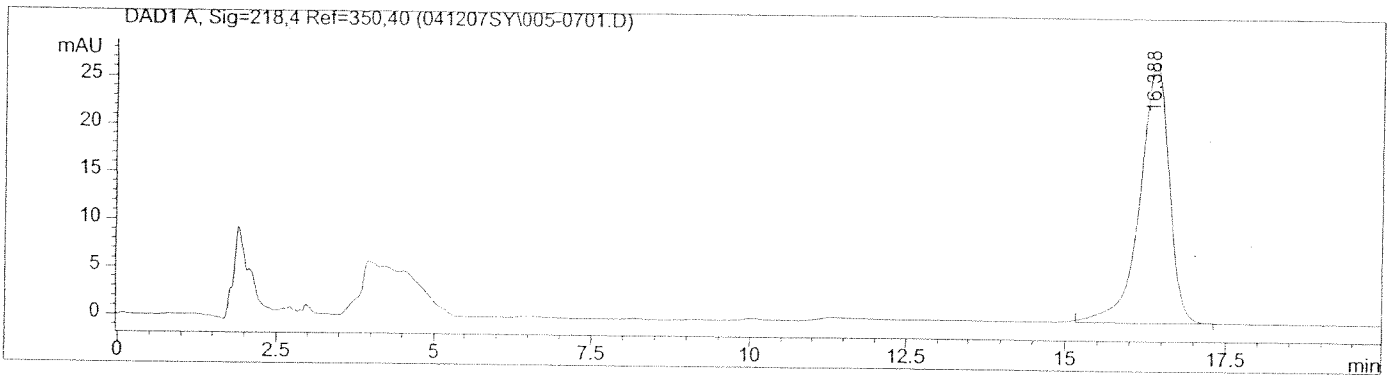
digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.388	BB	0.4792	856.10645	100.0000	digoxin

Totals : 856.10645

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Instrument 5 4/13/07 12:58:33 PM sly

Data File C:\HPCHEM\1\DATA\041207SY\006-0801.D Sample Name: 377410assay2

Injection Date : 4/12/07 7:03:58 PM Seq. Line : 8
Sample Name : 377410assay2 Vial : 6
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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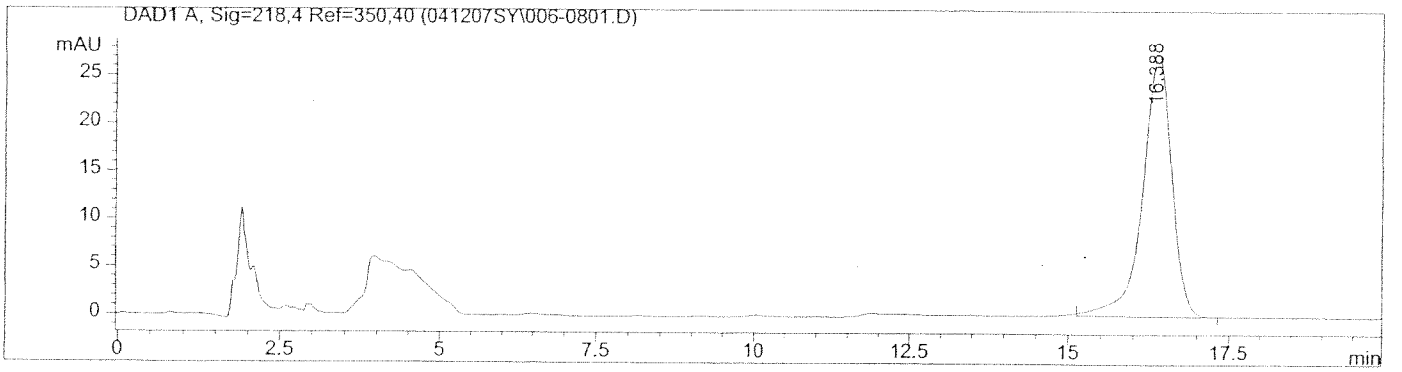
digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.388	BB	0.4787	860.05627	100.0000	digoxin

Totals : 860.05627

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\007-0901.D Sample Name: matrix spike

Injection Date : 4/12/07 7:25:25 PM Seq. Line : 9
Sample Name : matrix spike Vial : 7
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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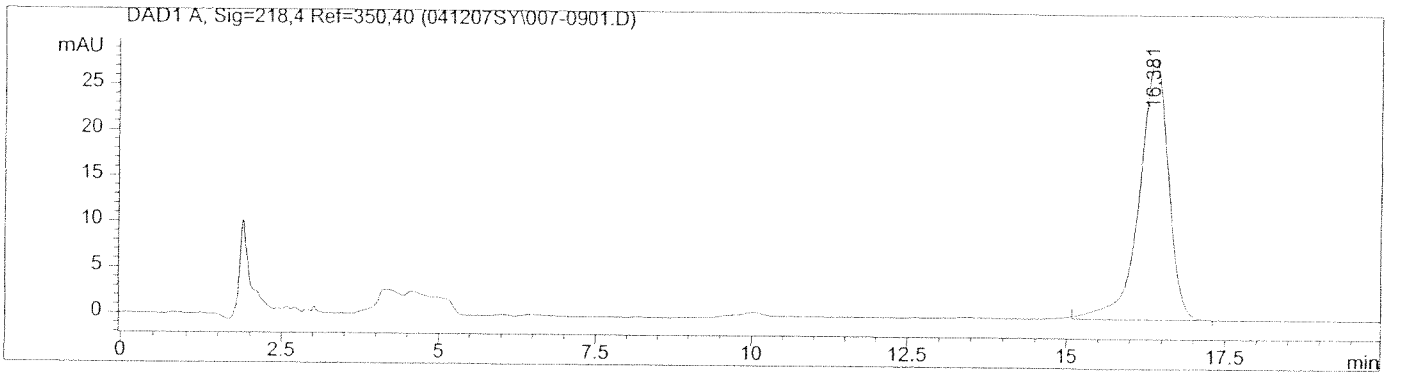
digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.381	BB	0.4789	903.54938	100.0000	digoxin

Totals : 903.54938

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\008-1001.D Sample Name: CU1

Injection Date	: 4/12/07 7:46:51 PM	Seq. Line	: 10
Sample Name	: CU1	Vial	: 8
Acq. Operator	: sly	Inj	: 1
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 37745
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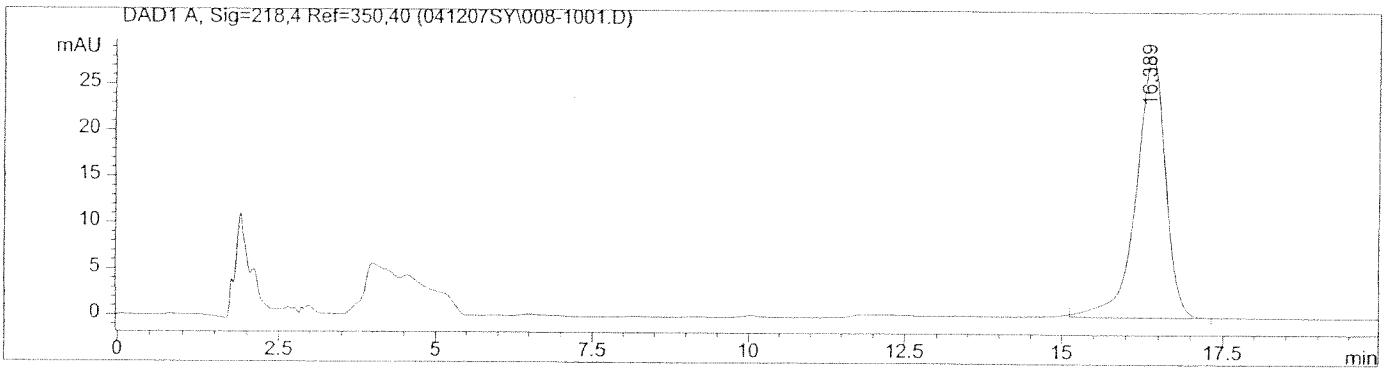
digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.389	BB	0.4792	890.91492	100.0000	digoxin

Totals : 890.91492

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\009-1101.D Sample Name: CU2

Injection Date : 4/12/07 8:08:20 PM Seq. Line : 11
Sample Name : CU2 Vial : 9
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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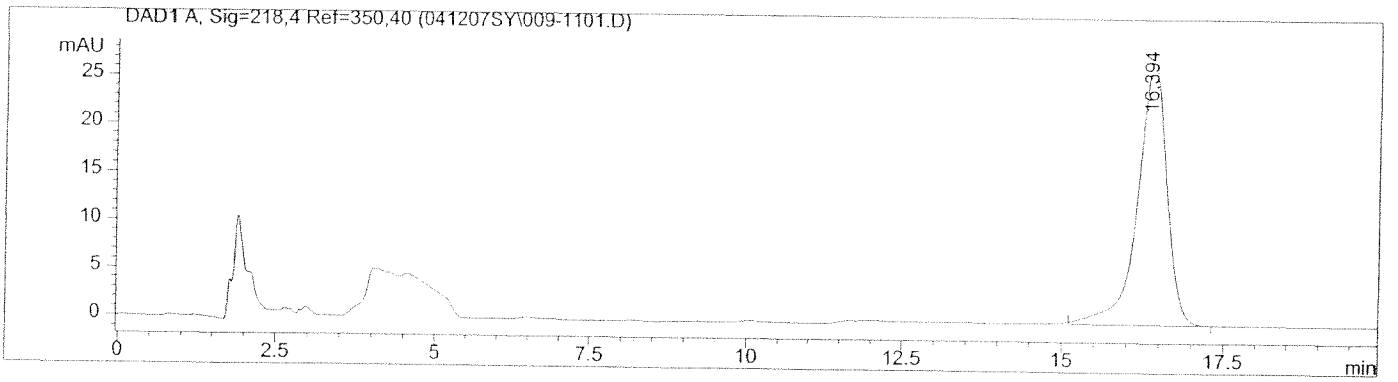
digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.394	BB	0.4777	862.61694	100.0000	digoxin

Totals : 862.61694

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\010-1201.D Sample Name: CU3

Injection Date : 4/12/07 8:29:49 PM Seq. Line : 12
Sample Name : CU3 Vial : 10
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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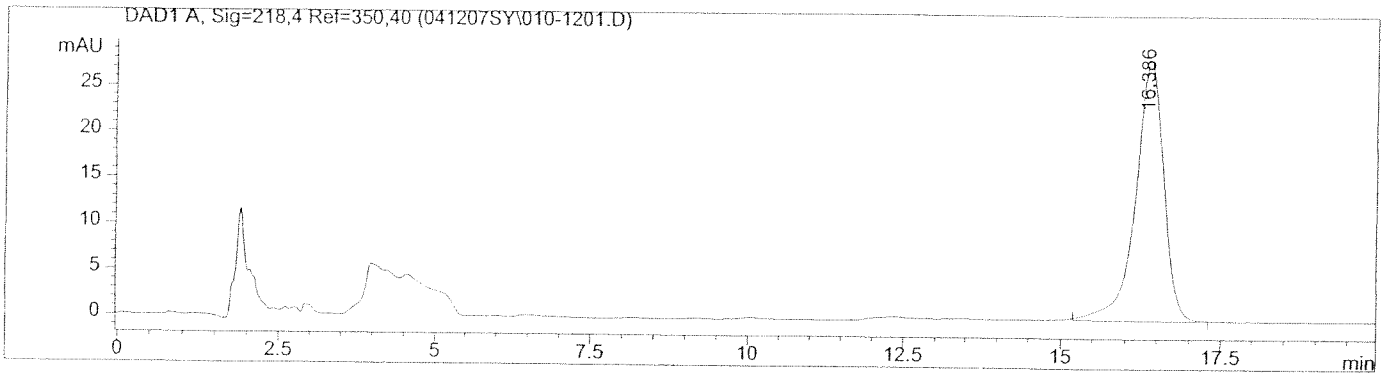
digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.386	BB	0.4711	880.40179	100.0000	digoxin

Totals : 880.40179

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\011-1301.D Sample Name: CU4

Injection Date	: 4/12/07 8:51:18 PM	Seq. Line	: 13
Sample Name	: CU4	Vial	: 11
Acq. Operator	: sly	Inj	: 1
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410
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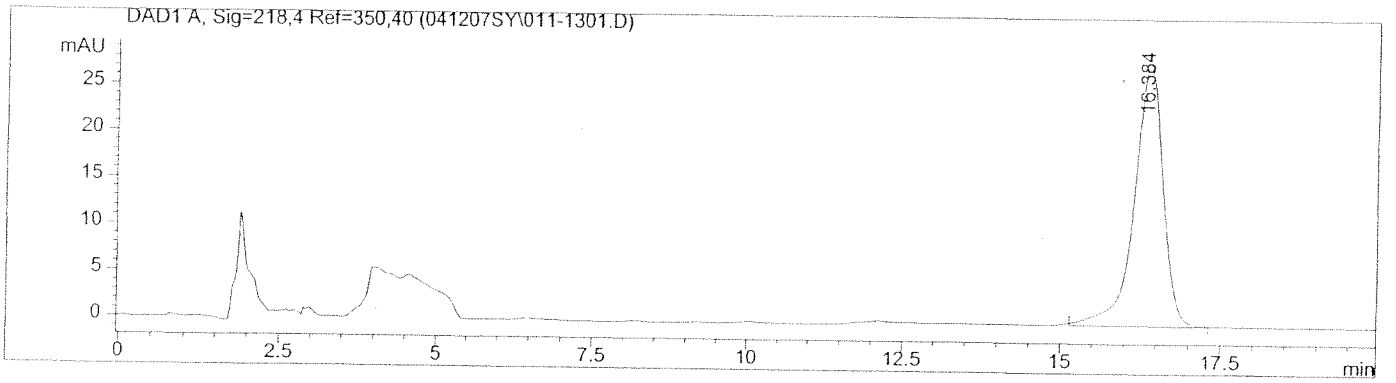
digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.384	BB	0.4747	881.50073	100.0000	digoxin
Totals :				881.50073		

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\012-1401.D Sample Name: CU5

Injection Date	: 4/12/07 9:12:44 PM	Seq. Line :	14
Sample Name	: CU5	Vial :	12
Acq. Operator	: sly	Inj :	1
		Inj Volume :	25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly		
	(modified after loading)		

Sample # 377410
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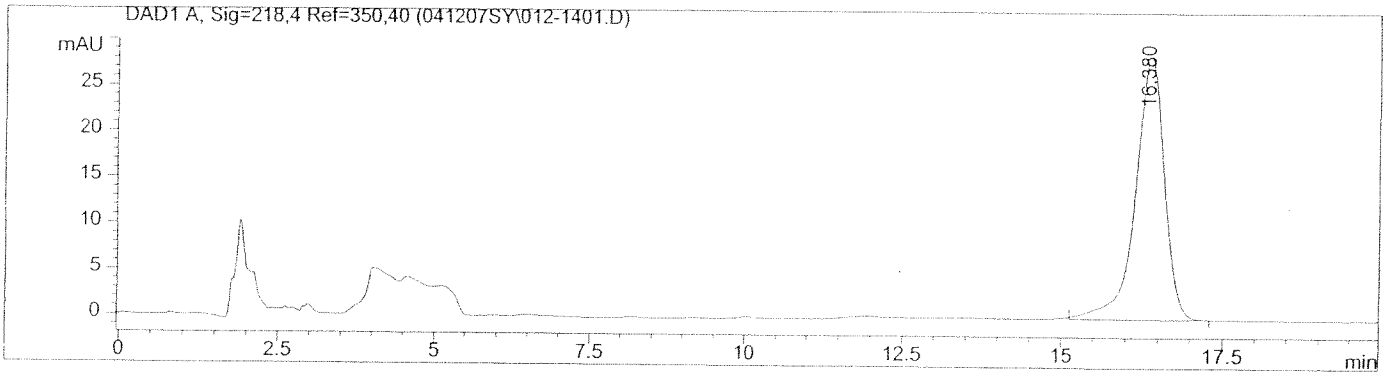
digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.380	BB	0.4738	892.34027	100.0000	digoxin
Totals :				892.34027		

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\003-1501.D Sample Name: CCV

Injection Date : 4/12/07 9:34:10 PM
Sample Name : CCV
Acq. Operator : sly

Seq. Line : 15
Vial : 3
Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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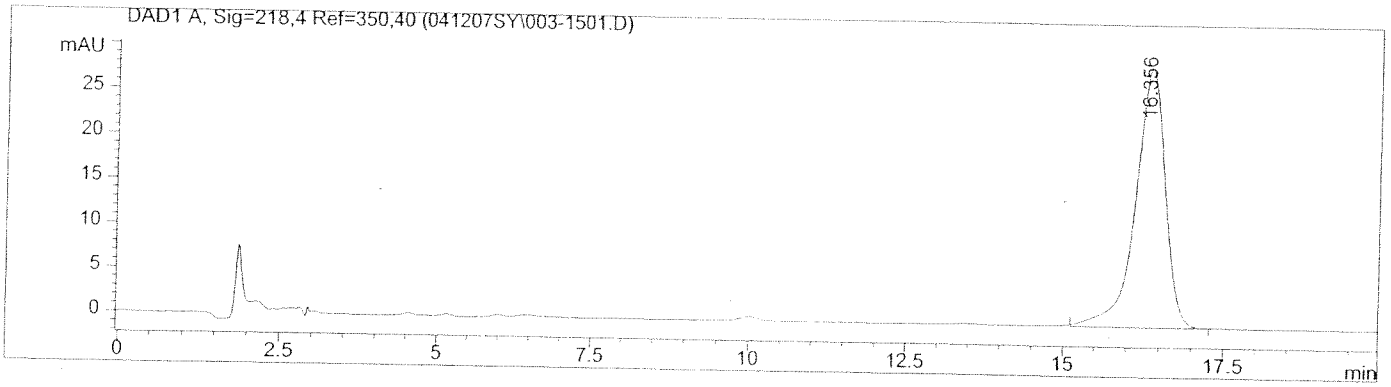
digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.356	BB	0.4865	924.38165	100.0000	digoxin

Totals : 924.38165

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Instrument 5 4/13/07 12:57:02 PM sly

Data File C:\HPCHEM\1\DATA\041207SY\013-1601.D Sample Name: CU6

Injection Date : 4/12/07 9:55:36 PM Seq. Line : 16
Sample Name : CU6 Vial : 13
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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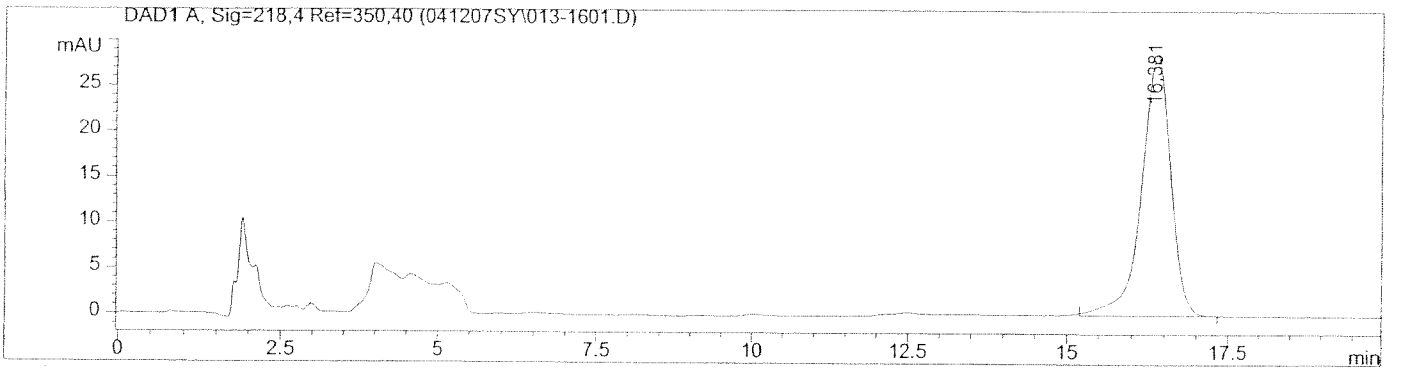
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.381	BB	0.4709	887.99988	100.0000	digoxin

Totals : 887.99988

Results obtained with enhanced integrator!
1 Warnings or Errors :

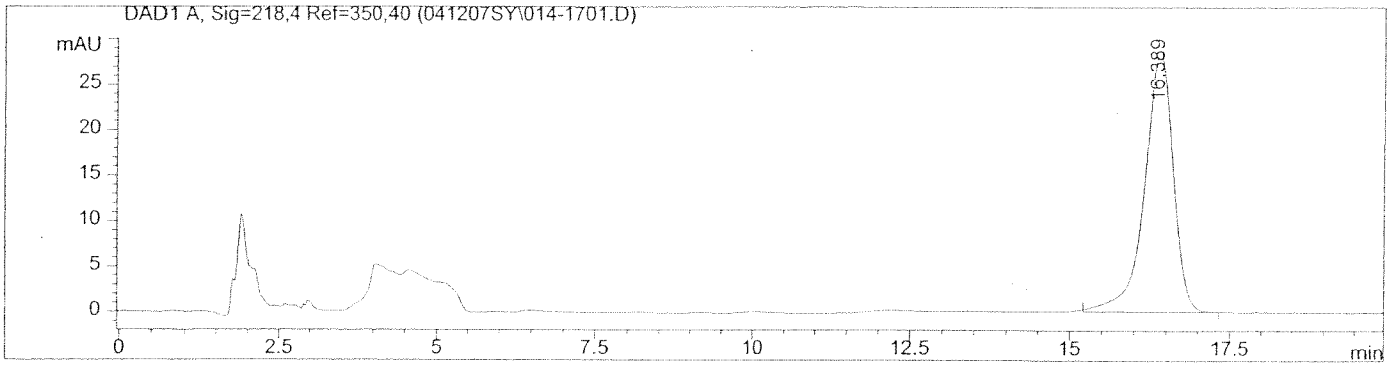
Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\014-1701.D Sample Name: CU7

Injection Date	: 4/12/07 10:17:02 PM	Seq. Line	: 17
Sample Name	: CU7	Vial	: 14
Acq. Operator	: sly	Inj	: 1
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410
Attachment A pg 35 of 44
SLY 5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.389	BB	0.4746	890.26398	100.0000	digoxin

Totals : 890.26398

Results obtained with enhanced integrator!
1 Warnings or Errors :

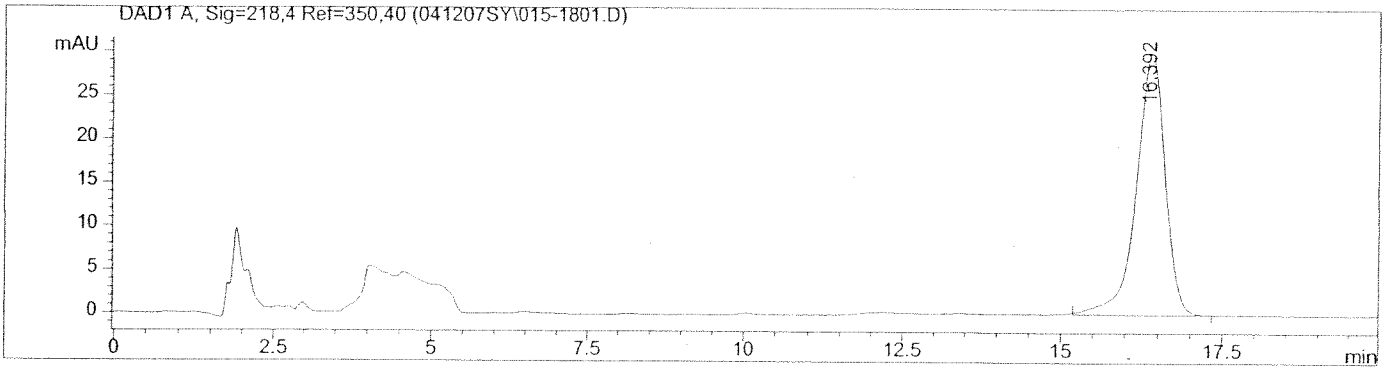
Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\015-1801.D Sample Name: CU8

Injection Date	: 4/12/07 10:38:28 PM	Seq. Line	: 18
Sample Name	: CU8	Vial	: 15
Acq. Operator	: sly	Inj	: 1
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410
Attachment A pg 36 of 44
SLY 5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.392	BB	0.4739	928.09546	100.0000	digoxin

Totals : 928.09546

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

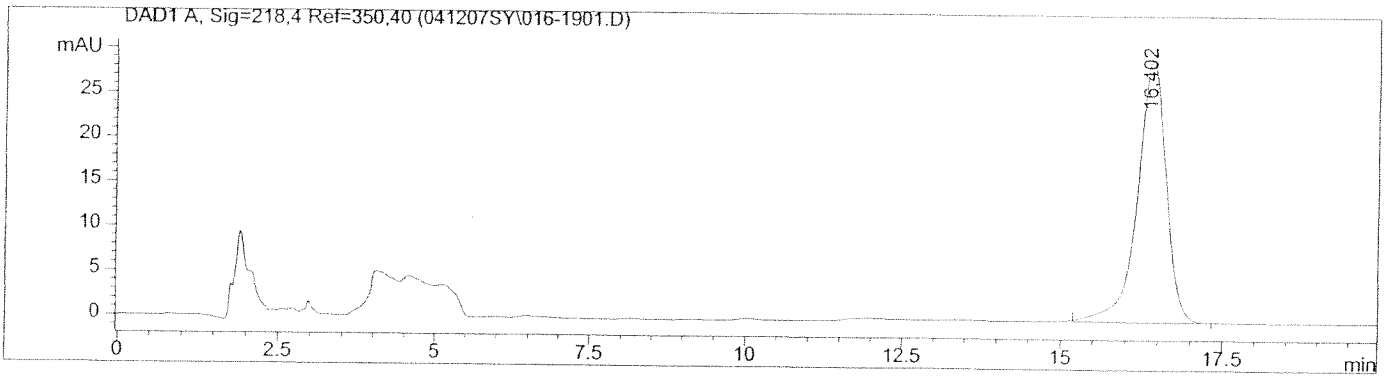
Data File C:\HPCHEM\1\DATA\041207SY\016-1901.D Sample Name: CU9

Injection Date : 4/12/07 10:59:55 PM Seq. Line : 19
Sample Name : CU9 Vial : 16
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
Attachment A pg 37 of 44
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.402	BB	0.4733	907.32068	100.0000	digoxin

Totals : 907.32068

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

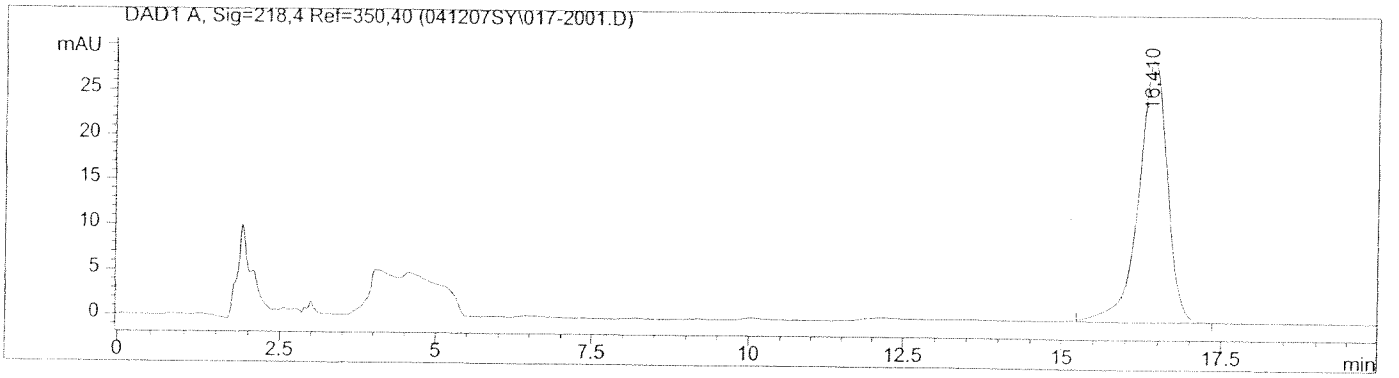
Data File C:\HPCHEM\1\DATA\041207SY\017-2001.D Sample Name: CU10

Injection Date : 4/12/07 11:21:22 PM Seq. Line : 20
Sample Name : CU10 Vial : 17
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 372410
Attachment A pg 38 of 44
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.410	BB	0.4688	897.28046	100.0000	digoxin

Totals : 897.28046

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Instrument 5 4/13/07 1:07:48 PM sly

Data File C:\HPCHEM\1\DATA\041207SY\003-2101.D Sample Name: CCV

Injection Date : 4/12/07 11:42:49 PM Seq. Line : 21
Sample Name : CCV Vial : 3
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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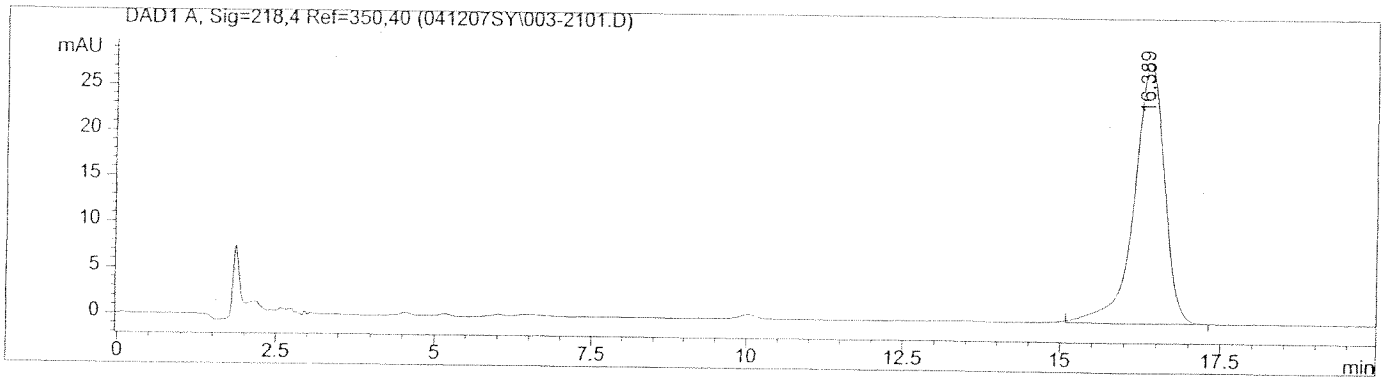
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.389	BB	0.4894	916.10974	100.0000	digoxin

Totals : 916.10974

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\001-2201.D Sample Name: blank

Injection Date	: 4/13/07 12:04:16 AM	Seq. Line :	22
Sample Name	: blank	Vial :	1
Acq. Operator	: sly	Inj :	1
		Inj Volume :	25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410
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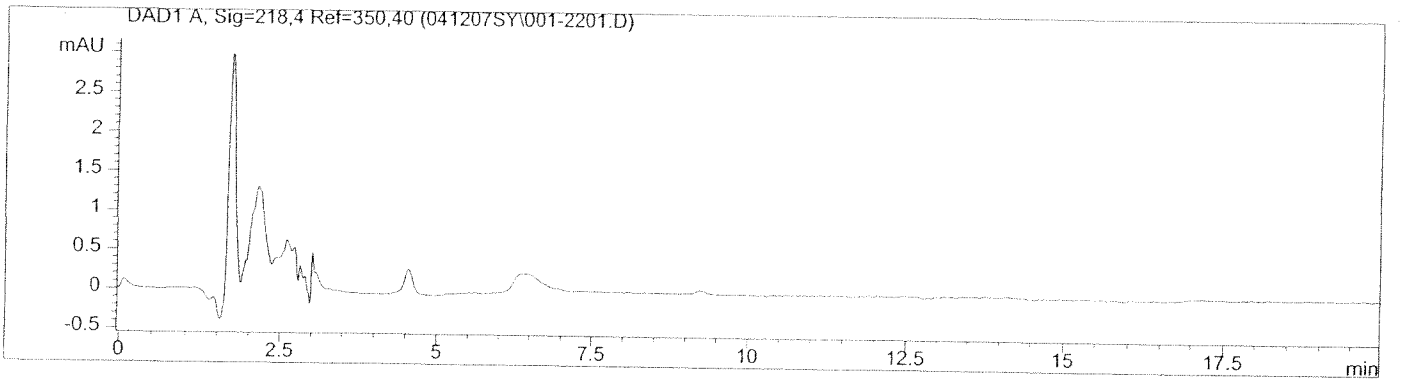
SLY 5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.352		0.0000	0.00000	0.0000	digoxin

Totals : 0.00000

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\018-2301.D Sample Name: MDL1

Injection Date : 4/13/07 12:25:45 AM Seq. Line : 23
Sample Name : MDL1 Vial : 18
Acq. Operator : sly Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
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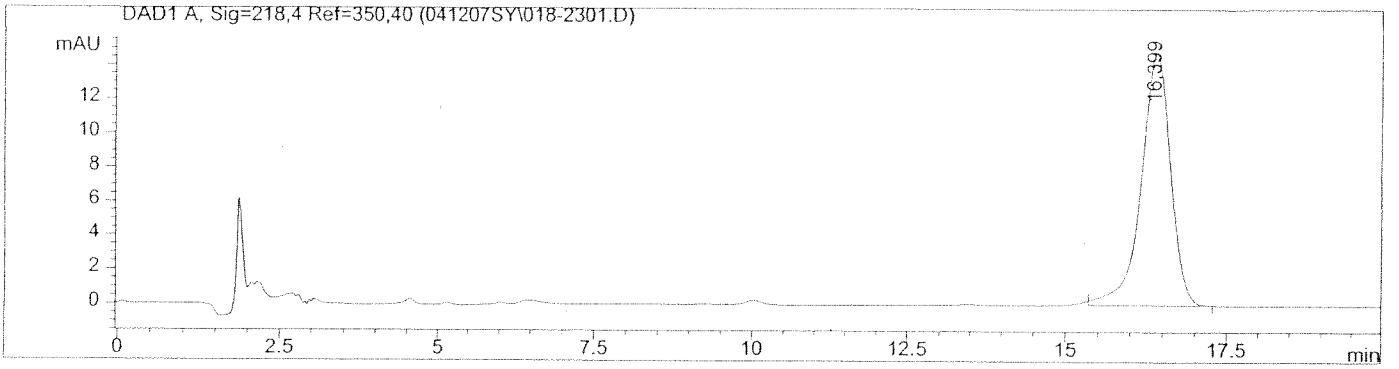
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.399	BB	0.4819	468.14490	100.0000	digoxin

Totals : 468.14490

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Data File C:\HPCHEM\1\DATA\041207SY\019-2401.D Sample Name: MDL2

Injection Date	: 4/13/07 12:47:14 AM	Seq. Line	: 24
Sample Name	: MDL2	Vial	: 19
Acq. Operator	: sly	Inj	: 1
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410
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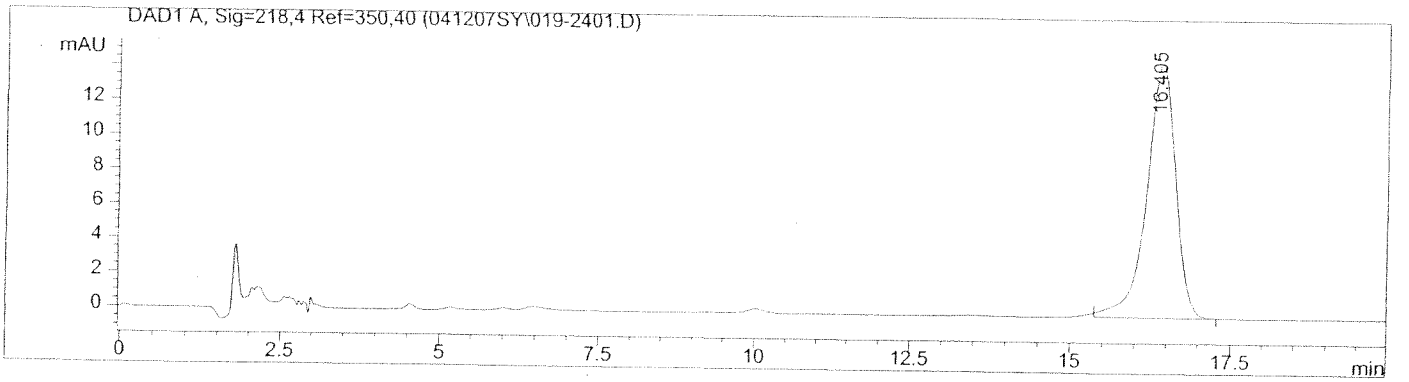
SLY 5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.405	BB	0.4801	462.41983	100.0000	digoxin
Totals :				462.41983		

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Instrument 5 4/13/07 1:09:23 PM sly

Data File C:\HPCHEM\1\DATA\041207SY\020-2501.D Sample Name: MDL3

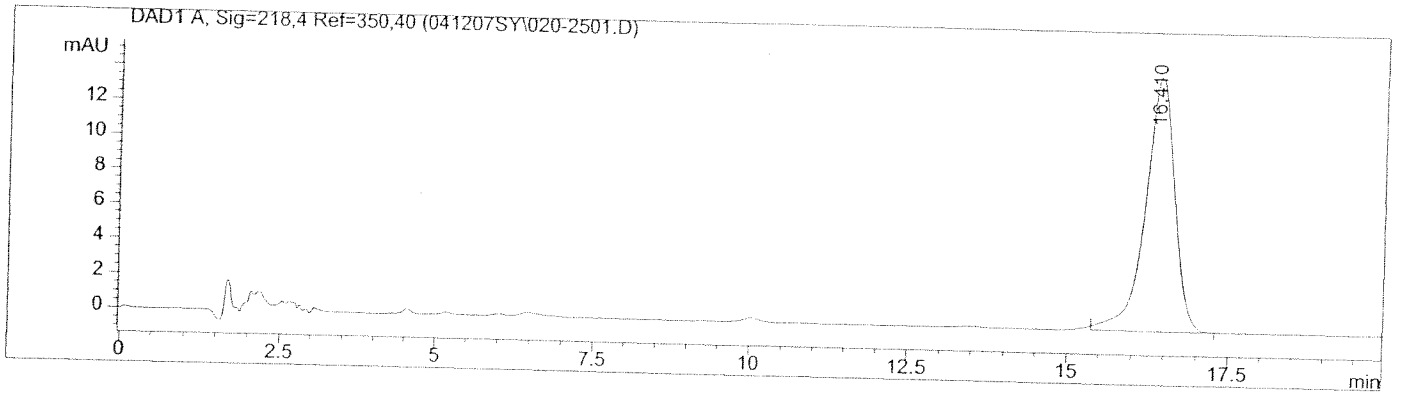
Injection Date : 4/13/07 1:08:42 AM
Sample Name : MDL3
Acq. Operator : sly

Seq. Line : 25
Vial : 20
Inj : 1
Inj Volume : 25 µl

Acq. Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/12/07 2:44:06 PM by sly
Analysis Method : C:\HPCHEM\1\METHODS\DIGOXIN.M
Last changed : 4/13/07 12:48:59 PM by sly
(modified after loading)

Sample # 377410
Attachment A pg 43 of 44
SLY 5-3-07

digoxin



Area Percent Report

Sorted By : Signal
Calib. Data Modified : 4/12/07 2:07:40 PM
Multiplier : 1.0000
Dilution : 1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.410	BB	0.4806	461.31964	100.0000	digoxin

Totals : 461.31964

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

Instrument 5 4/13/07 1:10:07 PM sly

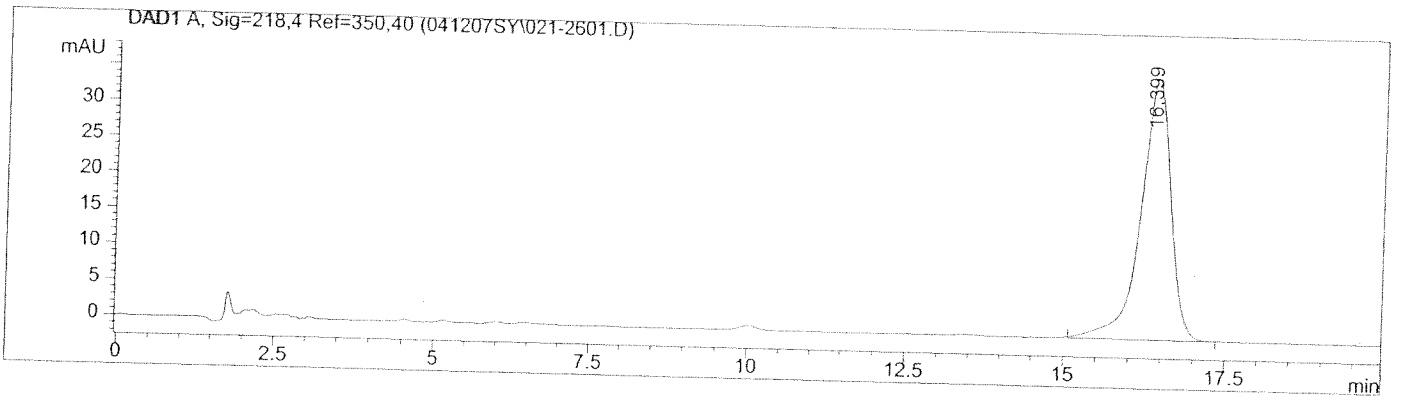
Data File C:\HPCHEM\1\DATA\041207SY\021-2601.D

Sample Name: high

Injection Date	: 4/13/07 1:30:12 AM	Seq. Line	: 26
Sample Name	: high	Vial	: 21
Acq. Operator	: sly	Inj	: 1
		Inj Volume	: 25 µl
Acq. Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/12/07 2:44:06 PM by sly		
Analysis Method	: C:\HPCHEM\1\METHODS\DIGOXIN.M		
Last changed	: 4/13/07 12:48:59 PM by sly (modified after loading)		

Sample # 377410
Attachment
SLY
Apg 44 of 44
5-3-07

digoxin



Area Percent Report

Sorted By	:	Signal
Calib. Data Modified	:	4/12/07 2:07:40 PM
Multiplier	:	1.0000
Dilution	:	1.0000

Signal 1: DAD1 A, Sig=218,4 Ref=350,40

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %	Name
1	5.187		0.0000	0.00000	0.0000	digoxigenin
2	16.399	BB	0.4896	1172.62061	100.0000	digoxin
Totals :				1172.62061		

Results obtained with enhanced integrator!
1 Warnings or Errors :

Warning : Calibrated compound(s) not found

377410
6-15-07
SCY

Attachment B

Organic Volatile Impurities

Chromatograms & Spectra

Simulate Run Sequence Tue Jun 12 12:53:15 2007

Instrument Name: Instrument #1
Sequence File: C:\MSDCHEM\1\SEQUENCE\OVI.S
Comment: ovi
Operator: sly
Data Path: C:\MSDCHEM\1\DATA\ovi\
Method Path: C:\MSDCHEM\1\METHODS\

Sample # 377410
Attachment B pg 1 of 33
SLY
6-15-07

Line	Type	Vial	DataFile	Method	Sample Name
1)	Sample	3	0612A01	OVI	WS1
2)	Sample	2	0612A02	ETOHCLN	etoh clean-up
3)	Sample	4	0612A03	OVI	WS2
4)	Sample	2	0612A04	ETOHCLN	etoh clean-up
5)	Sample	1	0612A05	OVI	blank
6)	Sample	2	0612A06	ETOHCLN	etoh clean-up
7)	Sample	5	0612A07	OVI	377410 digoxin
8)	Sample	2	0612A08	ETOHCLN	etoh clean-up
9)	Sample	6	0612A09	OVI	408376 alprostadil powder
10)	Sample	2	0612A10	ETOHCLN	etoh clean-up
11)	Sample	7	0612A11	OVI	414717 alprostadil liquid
12)	Sample	2	0612A12	ETOHCLN	etoh clean-up
13)	Sample	8	0612A13	OVI	420529 alprostadil liquid
14)	Sample	2	0612A14	ETOHCLN	etoh clean-up
15)	Sample	9	0612A15	OVI	412621 codeine
16)	Sample	2	0612A16	ETOHCLN	etoh clean-up
17)	Sample	3	0612A17	OVI	WS1
18)	Sample	2	0612A18	ETOHCLN	etoh clean-up
19)	Sample	10	0612A19	OVI	420501 nefazod
20)	Sample	2	0612A20	ETOHCLN	etoh clean-up
21)	Sample	11	0612A21	OVI	383890 naproxen
22)	Sample	2	0612A22	ETOHCLN	etoh clean-up
23)	Sample	12	0612A23	OVI	383890 spike 1
24)	Sample	2	0612A24	ETOHCLN	etoh clean-up
25)	Sample	13	0612A25	OVI	383891 naproxen
26)	Sample	2	0612A26	ETOHCLN	etoh clean-up
27)	Sample	14	0612A27	OVI	383891 spike 2
28)	Sample	2	0612A28	ETOHCLN	etoh clean-up
29)	Sample	3	0612A29	OVI	WS1
30)	Sample	2	0612A30	ETOHCLN	etoh clean-up
31)	Sample	15	0612A31	OVI	408372 naproxen
32)	Sample	2	0612A32	ETOHCLN	etoh clean-up
33)	Sample	16	0612A33	OVI	409673 naproxen
34)	Sample	2	0612A34	ETOHCLN	etoh clean-up
35)	Sample	17	0612A35	OVI	409674 naproxen
36)	Sample	2	0612A36	ETOHCLN	etoh clean-up
37)	Sample	18	0612A37	OVI	423339 naproxen
38)	Sample	2	0612A38	ETOHCLN	etoh clean-up
39)	Sample	19	0612A39	OVI	423340 naproxen
40)	Sample	2	0612A40	ETOHCLN	etoh clean-up
41)	Sample	3	0612A41	OVI	WS1
42)	Sample	2	0612A42	ETOHCLN	etoh clean-up
43)	Sample	20	0612A43	OVI	396200 desmopressin
44)	Sample	2	0612A44	ETOHCLN	etoh clean-up
45)	Sample	21	0612A45	OVI	420503 desmopressin
46)	Sample	2	0612A46	ETOHCLN	etoh clean-up
47)	Sample	3	0612A47	OVI	WS1
48)	Sample	2	0612A48	ETOHCLN	etoh clean-up

Agilent GC-MS
GC 6890 FDA#1700647
MS 5973 FDA#1700646

Bytes Needed: 2400000 Space on drive C: 1527685123
Sequence Verification Done!

TOPLEVEL PARAMETERS

Method Information For: C:\MSDCHEM\1\METHODS\OVI.M

od Sections To Run:

(X) Save Copy of Method With Data
( ) Pre-Run Cmd/Macro =
(X) Data Acquisition
(X) Data Analysis
( ) Post-Run Cmd/Macro =

Sample # 377413
Attachment B pg 2 of 33
SLY 6-15-07

Method Comments:
OVI

END OF TOPLEVEL PARAMETERS

INSTRUMENT CONTROL PARAMETERS

Sample Inlet: GC
Injection Source: GC ALS
Mass Spectrometer: Enabled

6890 GC METHOD

OVEN
Initial temp: 40 'C (On) Maximum temp: 340 'C
Initial time: 5.00 min Equilibration time: 0.10 min
Ramps:

#	Rate	Final temp	Final time
1	2.00	80	0.00
2	10.00	150	0.00
3	50.00	260	0.00
4	0.0(Off)		

Post temp: 40 'C
Post time: 0.00 min
Run time: 34.20 min

NT INLET (UNKNOWN) BACK INLET ()
ode: Splitless
Initial temp: 70 'C (On)

Pressure: 1.32 psi (On)
Purge flow: 50.0 mL/min
Purge time: 1.00 min
Total flow: 53.4 mL/min
Gas saver: On
ver flow: 20.0 mL/min
aver time: 3.00 min
Gas type: Helium

COLUMN 1
Capillary Column
Model Number: Restek RTx-5MS
5% diphenyl-95%dimethylpolysiloxane
Max temperature: 350 'C
Nominal length: 30.0 m
Nominal diameter: 250.00 um
Nominal film thickness: 0.25 um
Mode: constant flow
Initial flow: 0.5 mL/min
Nominal init pressure: 1.33 psi
Average velocity: 27 cm/sec
t: Front Inlet
Outlet: MSD
Outlet pressure: vacuum

COLUMN 2
(not installed)

Sample # 377410
Attachment B pg 3 of 33
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FRONT DETECTOR (NO DET)

BACK DETECTOR (NO DET)

SIGNAL 1
a rate: 20 Hz
ype: test plot
Save Data: Off
Zero: 0.0 (Off)
Range: 0
Fast Peaks: Off
Attenuation: 0

SIGNAL 2
Data rate: 20 Hz
Type: test plot
Save Data: Off
Zero: 0.0 (Off)
Range: 0
Fast Peaks: Off
Attenuation: 0

UMN COMP 1
(No Detectors Installed)

COLUMN COMP 2
(No Detectors Installed)

THERMAL AUX 2
Use: MSD Transfer Line Heater
Description: Transfer Line
Initial temp: 280 'C (On)
Initial time: 0.00 min

#	Rate	Final temp	Final time
1	0.0(Off)		

POST RUN
Post Time: 0.00 min

TIME TABLE

e	Specifier	Parameter & Setpoint

7673 Injector

Front Injector:

Sample Washes	2
Sample Pumps	3
Injection Volume	1.0 microliters
Syringe Size	10.0 microliters
PostInj Solvent A Washes	4
PostInj Solvent B Washes	4
Viscosity Delay	0 seconds
Plunger Speed	Fast
PreInjection Dwell	0.00 minutes
PostInjection Dwell	0.00 minutes
Sampling Depth	0.4 mm

Sample # 377410
Attachment B pg 4 of 33
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Back Injector:
No parameters specified

MS ACQUISITION PARAMETERS

General Information

Tune File : atune.u
Acquistion Mode : Scan

Information

Solvent Delay : 3.00 min

EM Absolute : False
EM Offset : 0
Resulting EM Voltage : 1482.4

[Scan Parameters]

Low Mass : 30.0
High Mass : 175.0
Threshold : 100
Sample # : 2 A/D Samples 4
Plot 2 low mass : 35.0
Plot 2 high mass : 545.0

[MSZones]

MS Quad : 150 C maximum 200 C
MS Source : 230 C maximum 250 C

END OF MS ACQUISITION PARAMETERS

File : C:\MSDCHEM\1\DATA\OVI\0612A01.D
Operator : sly
Acquired : 12 Jun 2007 14:31 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS1
Misc Info :
Vial Number: 3

Sample # 377410
Attachment B pg 5 of 33
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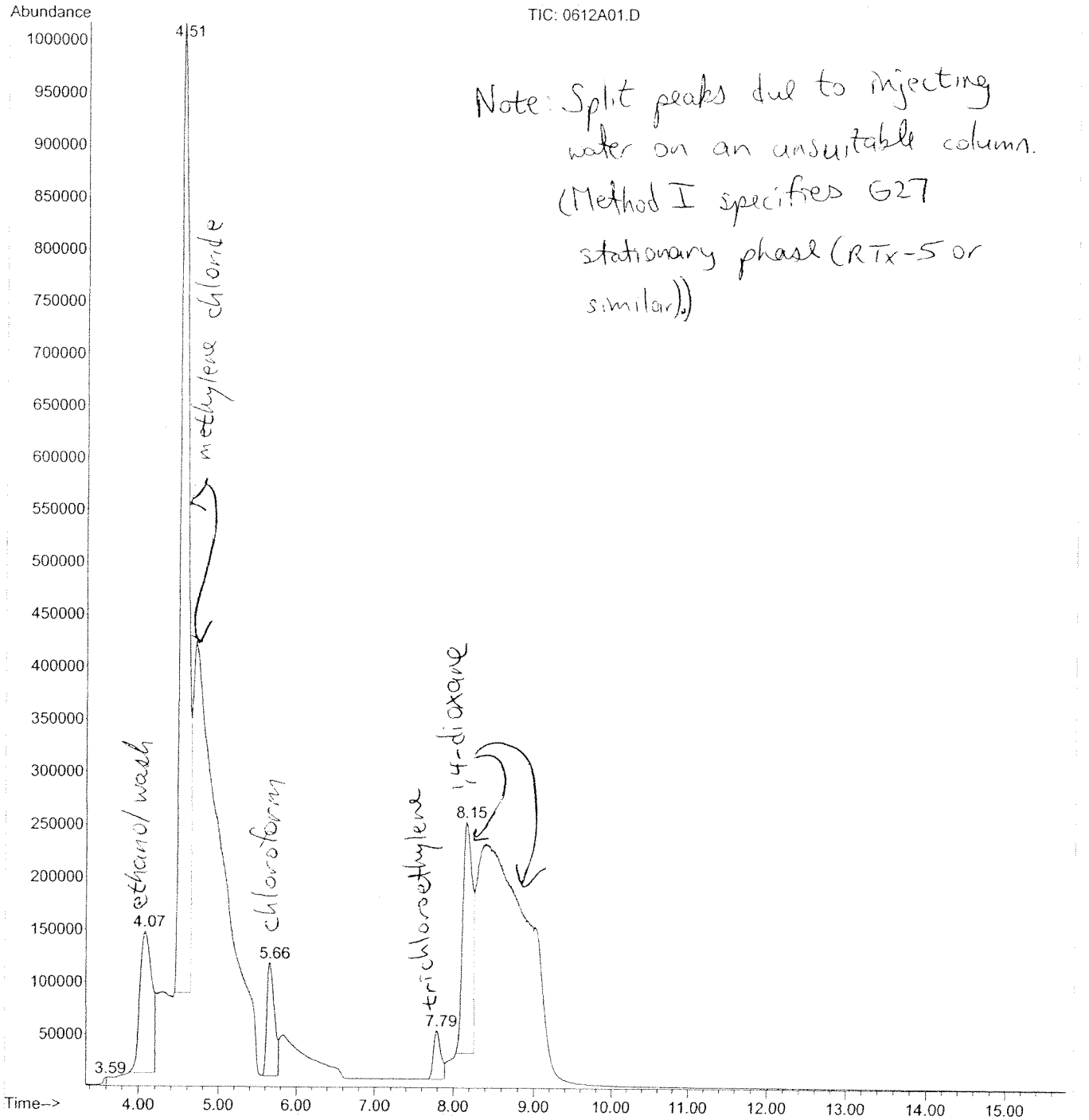
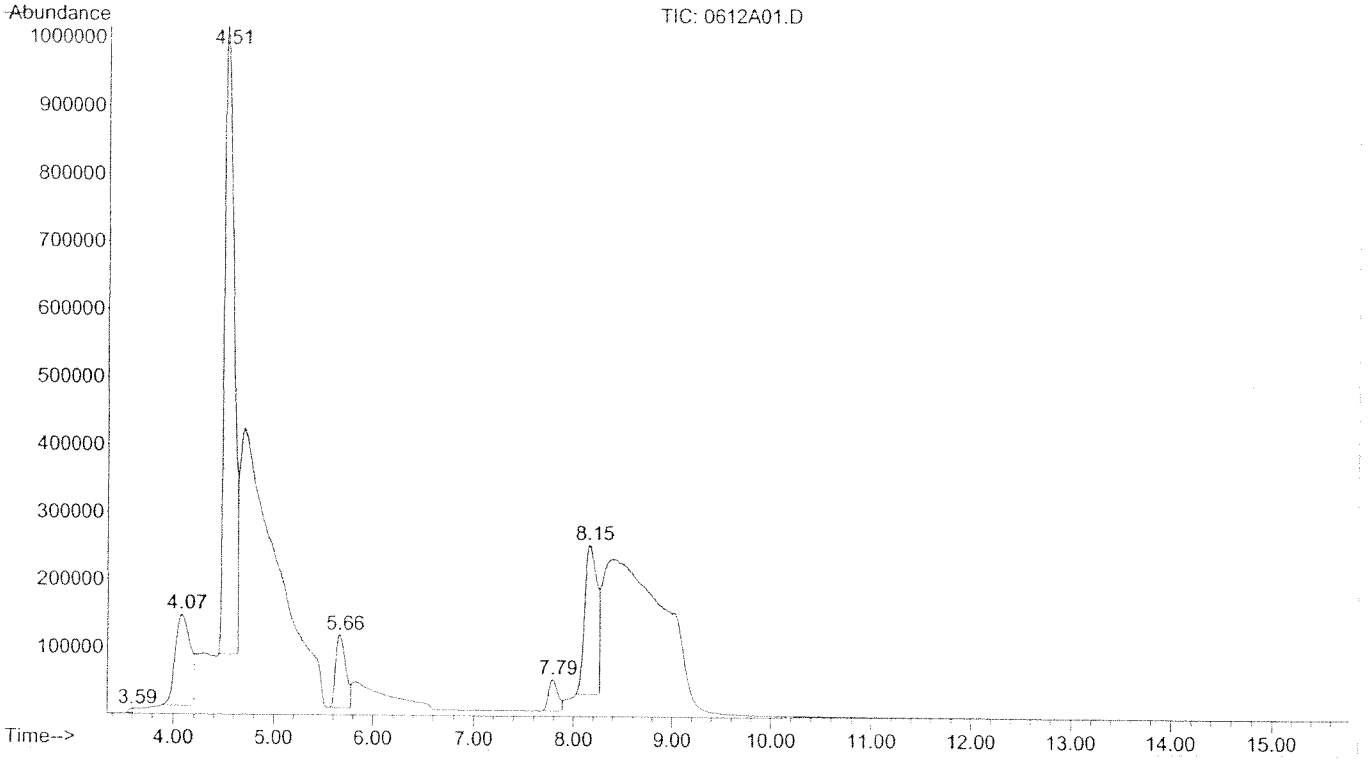
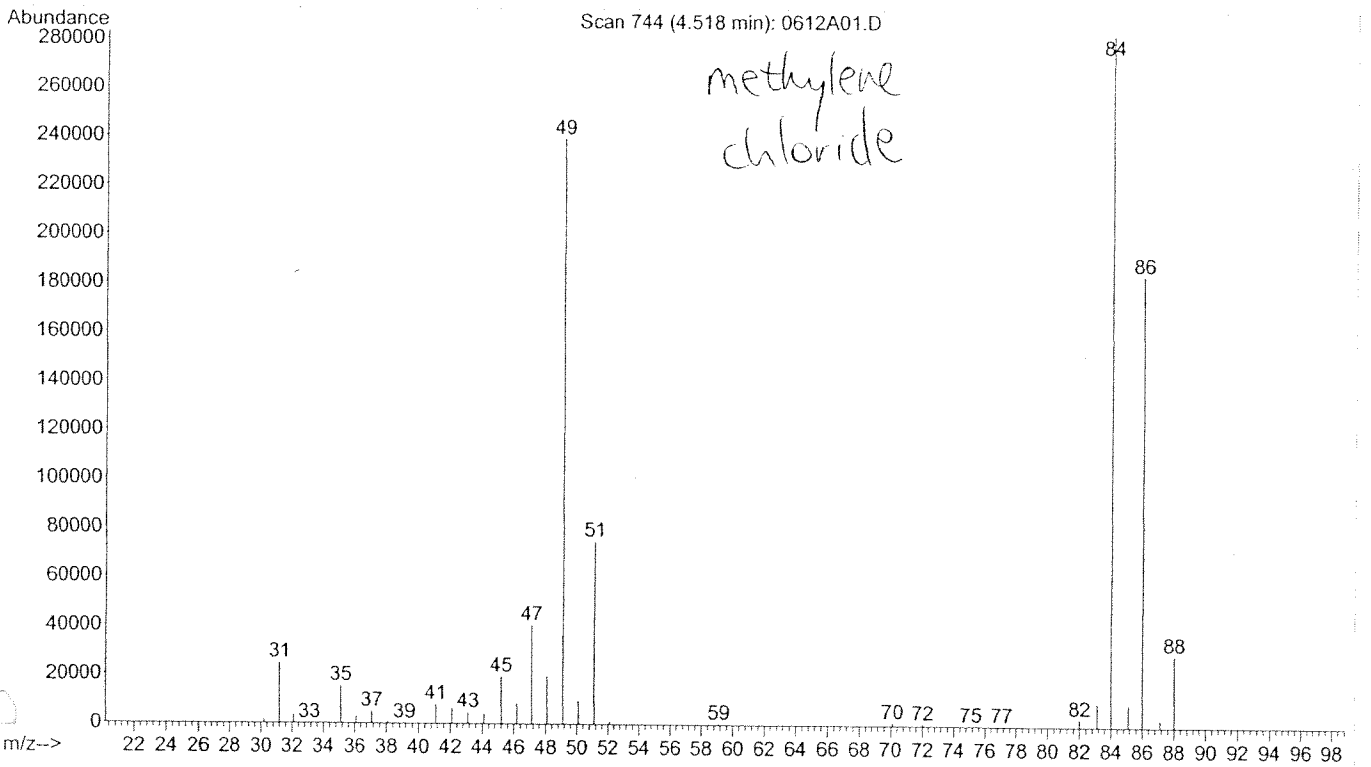


Note: Split peaks due to injecting water on an unsuitable column. (Method I specifies G27 stationary phase (RTx-5 or similar).)

File : C:\MSDCHEM\1\DATA\OVI\0612A01.D
Operator : sly
Acquired : 12 Jun 2007 14:31 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS1
Misc Info :
Vial Number: 3

Sample # 37740 of 33
Attachment B pg 6
SLY 6-15-07





File : C:\MSDCHEM\1\DATA\OVI\0612A01.D
Operator : sly
Acquired : 12 Jun 2007 14:31 using AcqMethod OVI
Instrument : Instrumen
`ample Name: WS1
Misc Info :
Vial Number: 3

Sample # 377410
Attachment B pg 7 of 33
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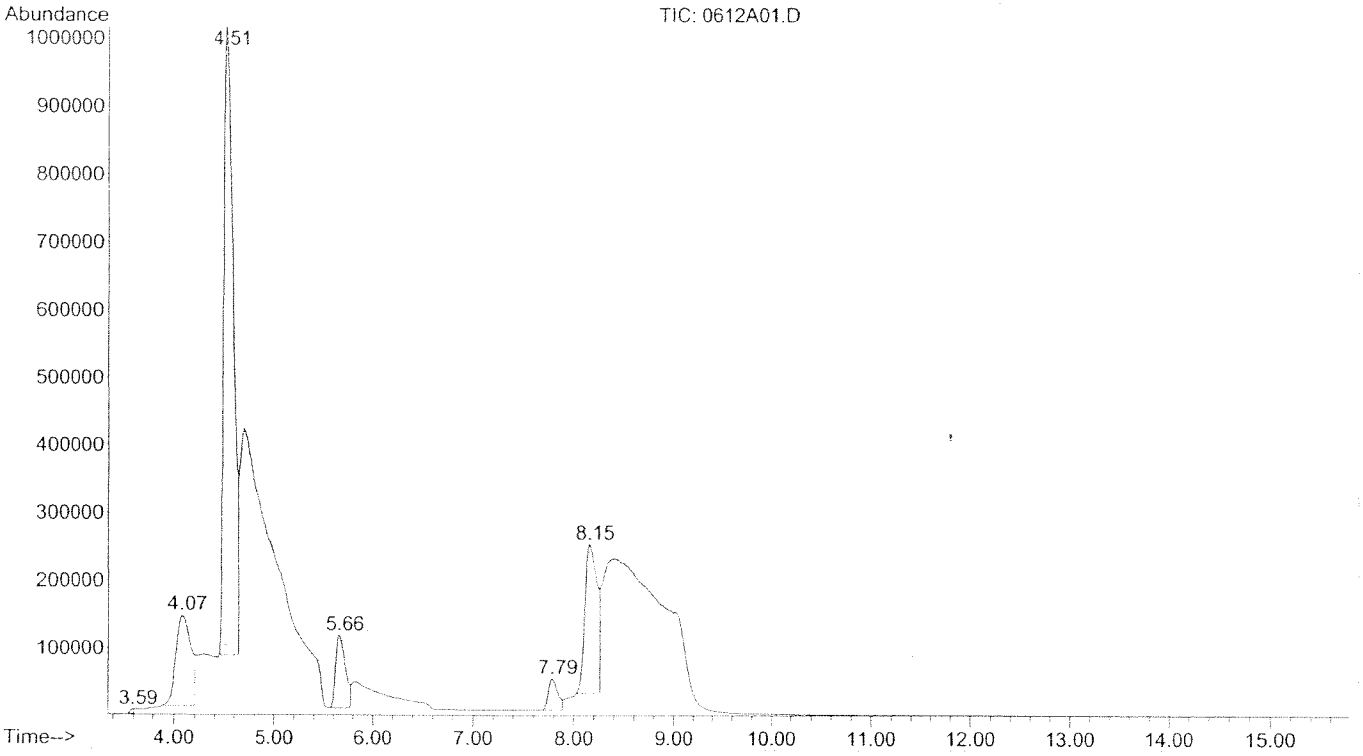

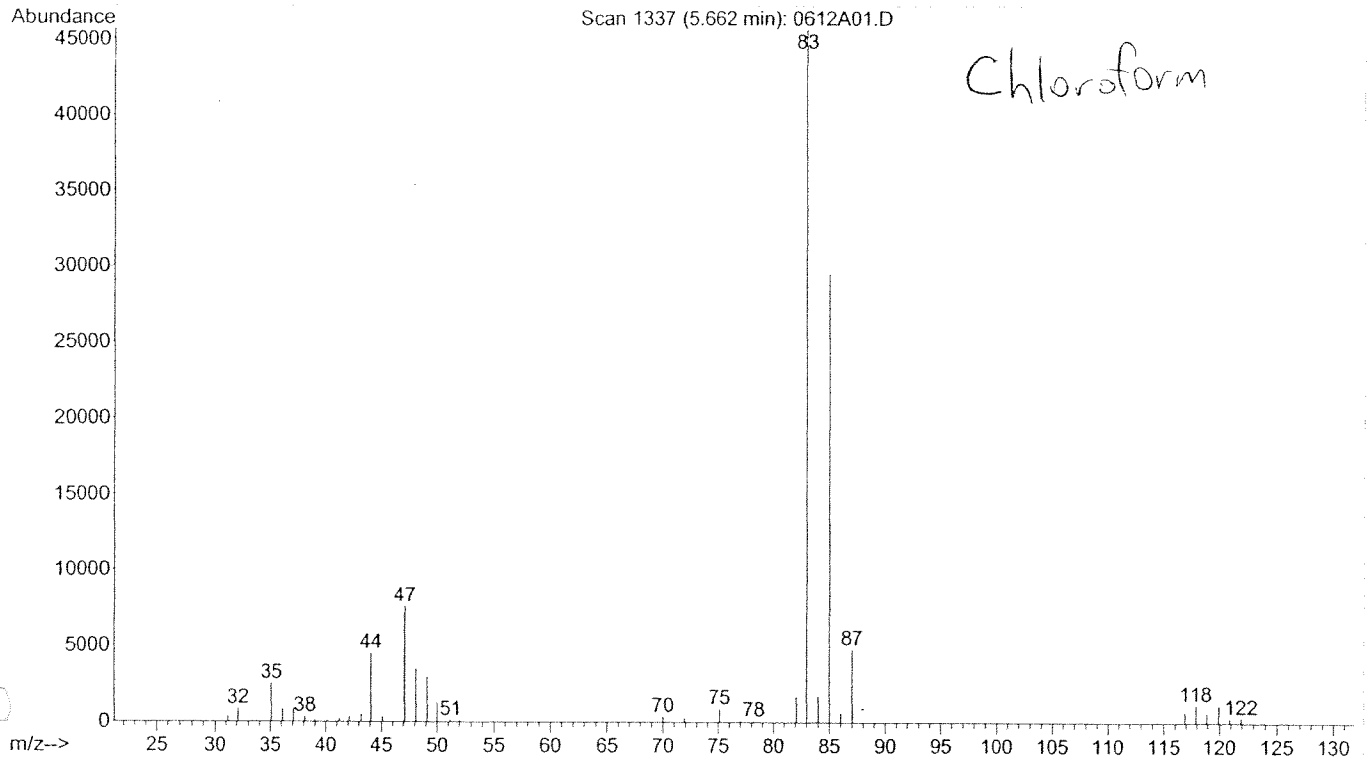

Chloroform

File : C:\MSDCHEM\1\DATA\OVI\0612A01.D
Operator : sly
Acquired : 12 Jun 2007 14:31 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS1
Misc Info :
Vial Number: 3

Sample # 377410
Attachment B pg 8 of 33
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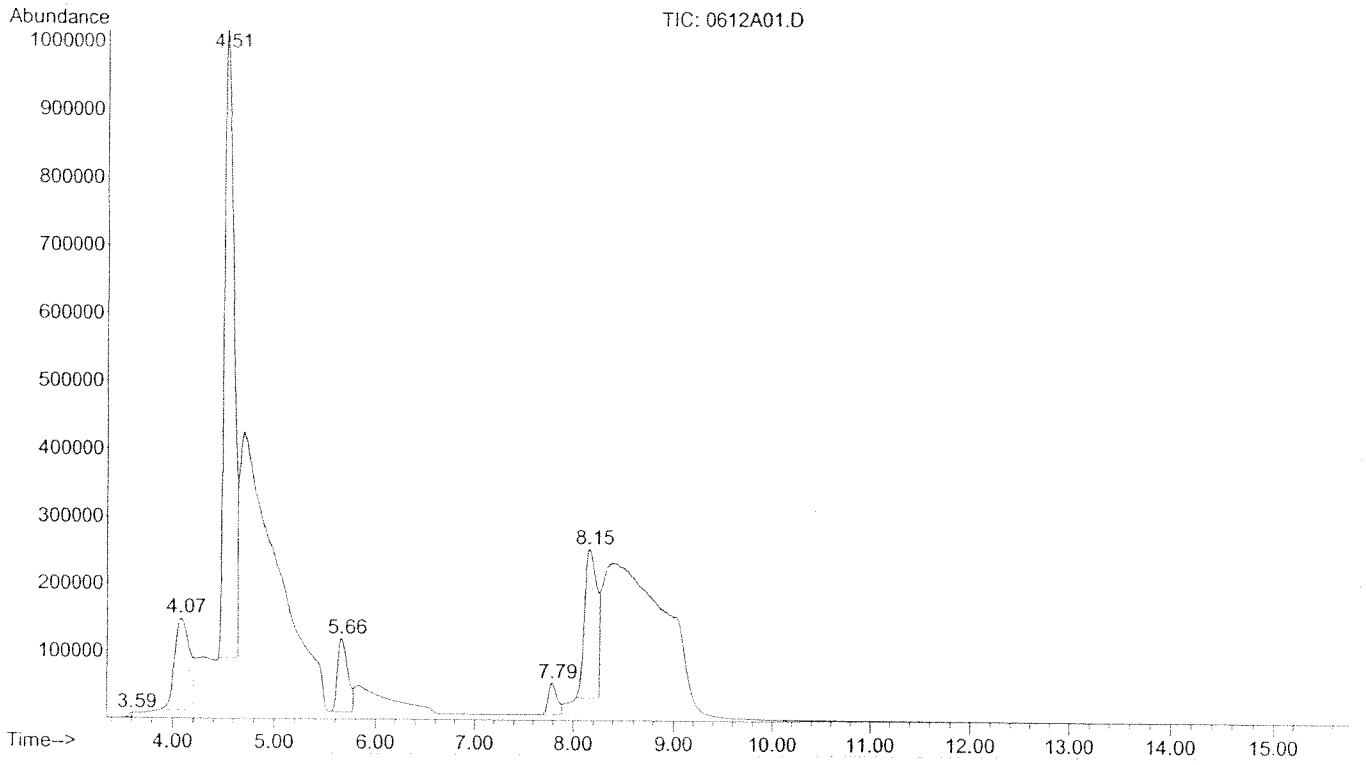

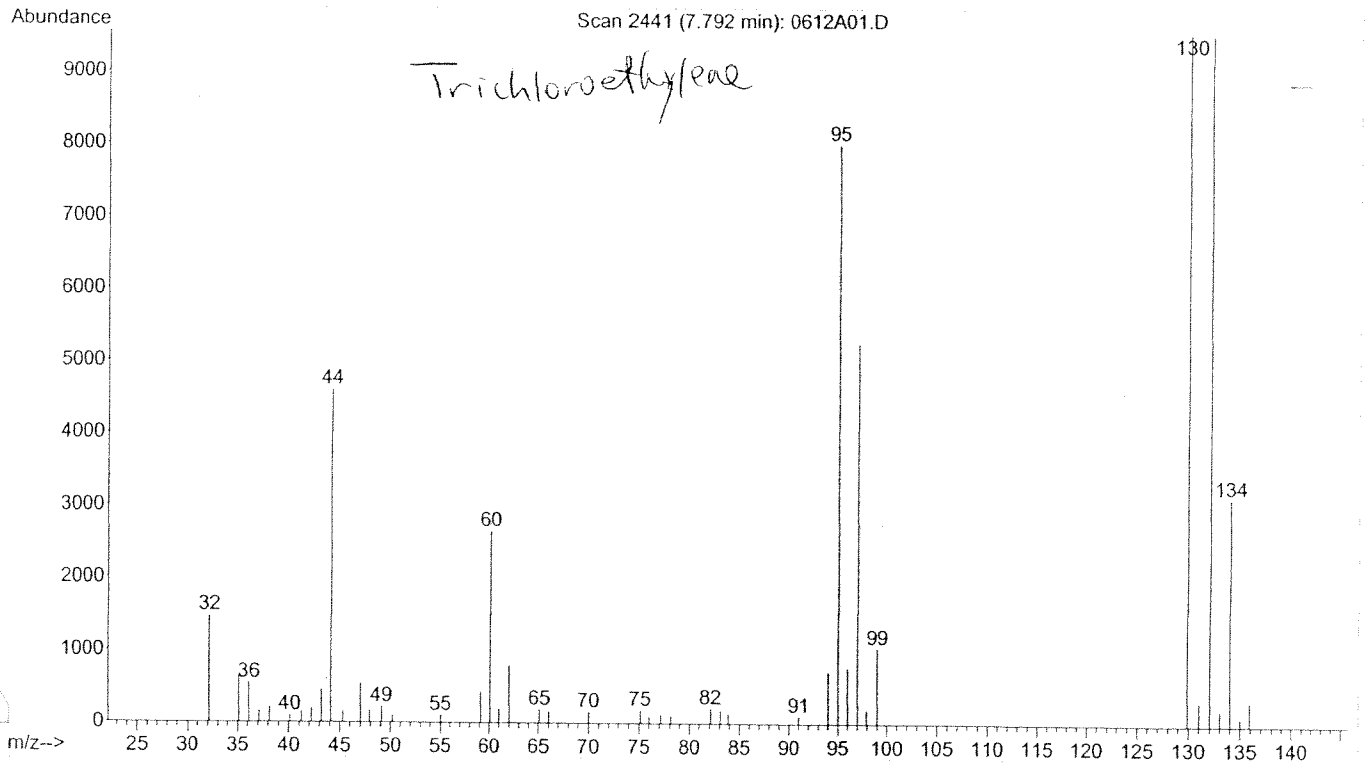

File : C:\MSDCHEM\1\DATA\OVI\0612A01.D
Operator : sly
Acquired : 12 Jun 2007 14:31 using AcqMethod OVI
Instrument : Instrumen
ample Name: WS1
Misc Info :
Vial Number: 3

Sample # 377410
Attachment B pg 9 of 33
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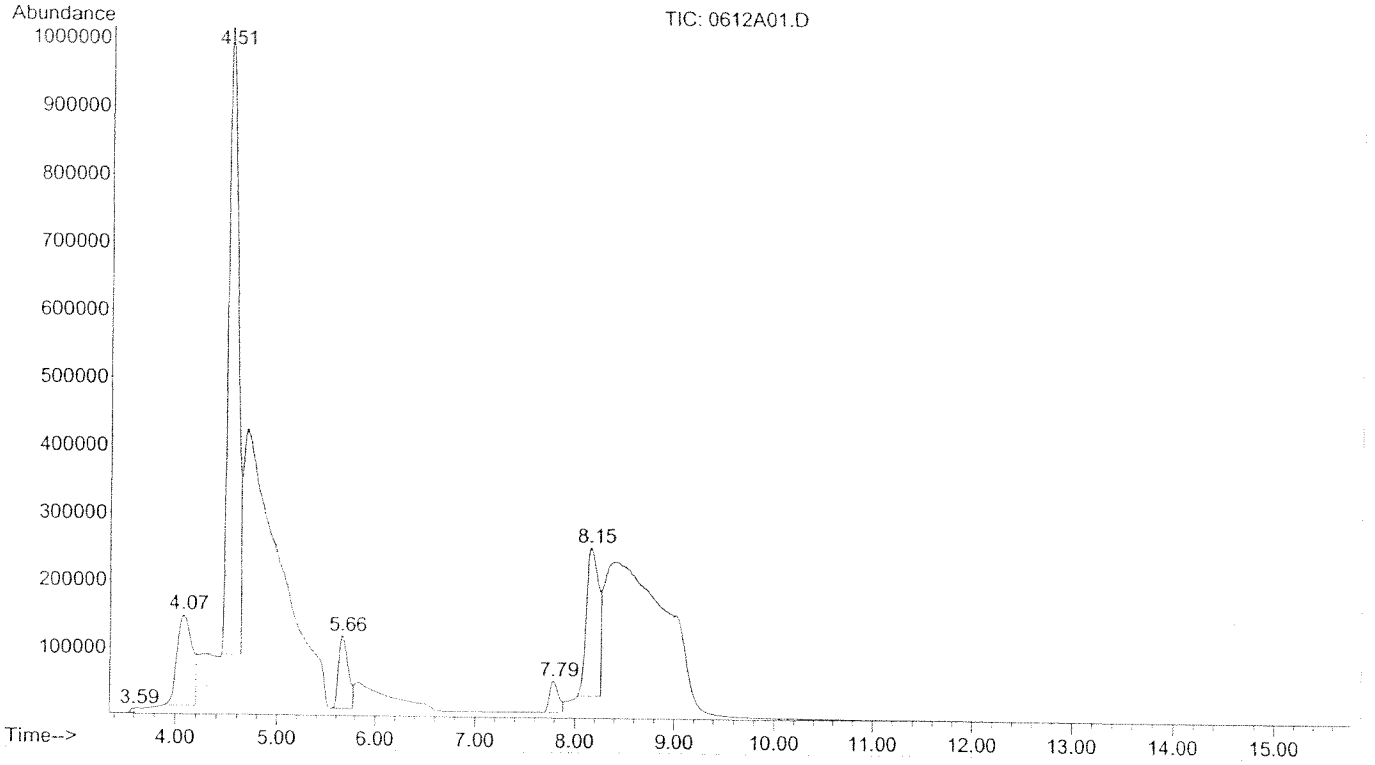

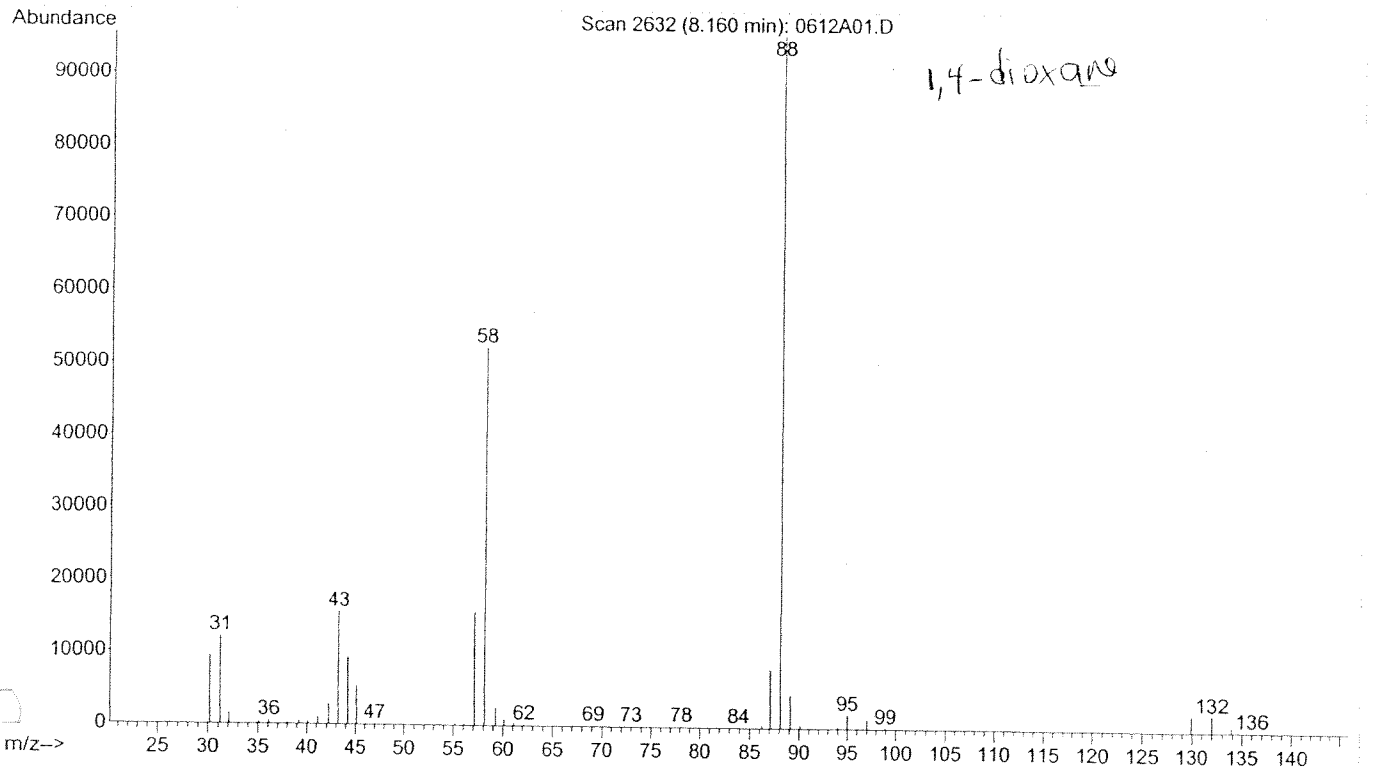

File : C:\MSDCHEM\1\DATA\OVI\0612A03.D
Operator : sly
Acquired : 12 Jun 2007 15:32 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS2
Misc Info :
Vial Number: 4

Sample # 37710
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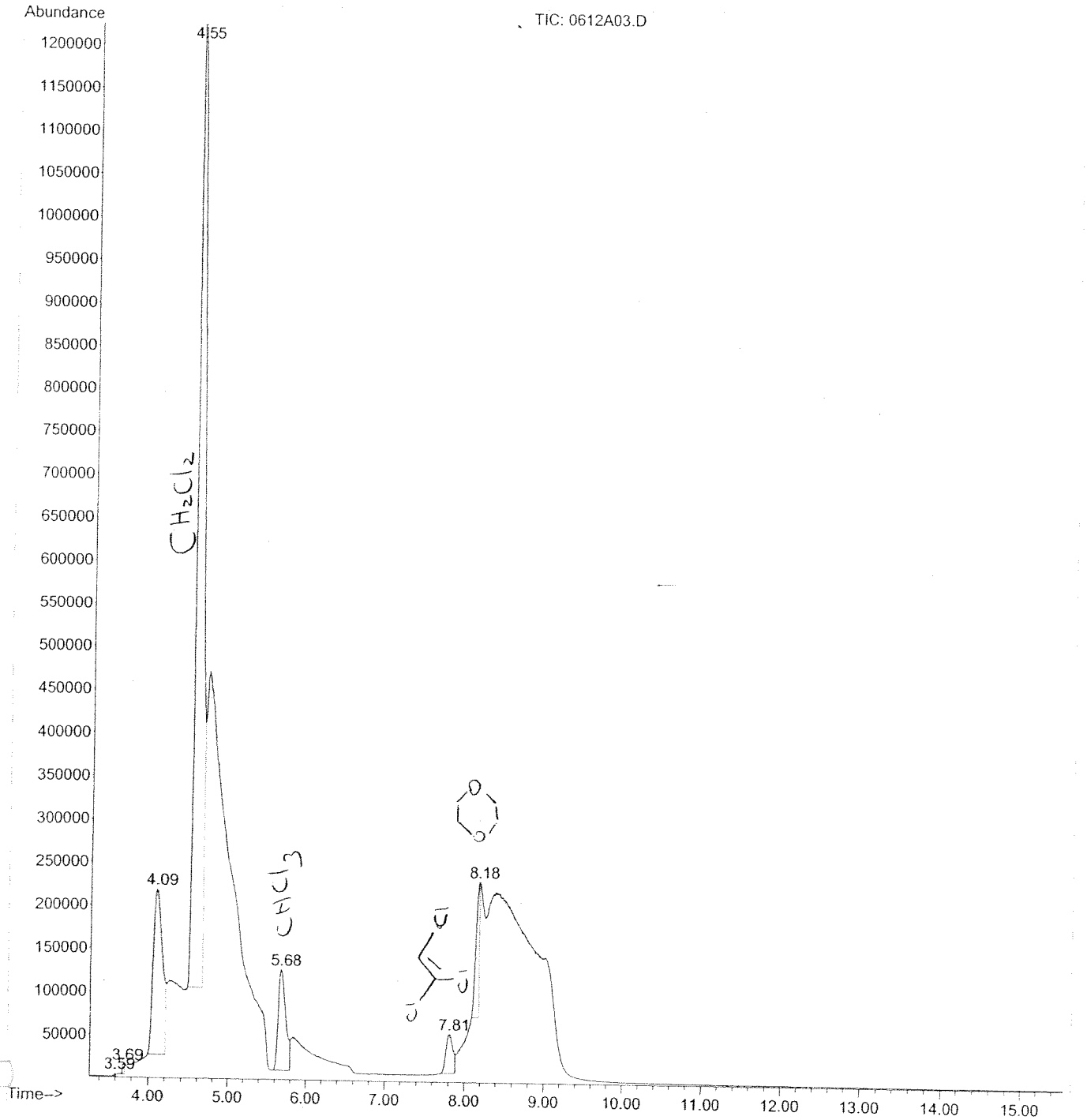

File : C:\MSDCHEM\1\DATA\OVI\0612A07.D
Operator : sly
Acquired : 13 Jun 2007 11:21 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 377410 digoxin
Misc Info :
Vial Number: 5

Sample # 377410
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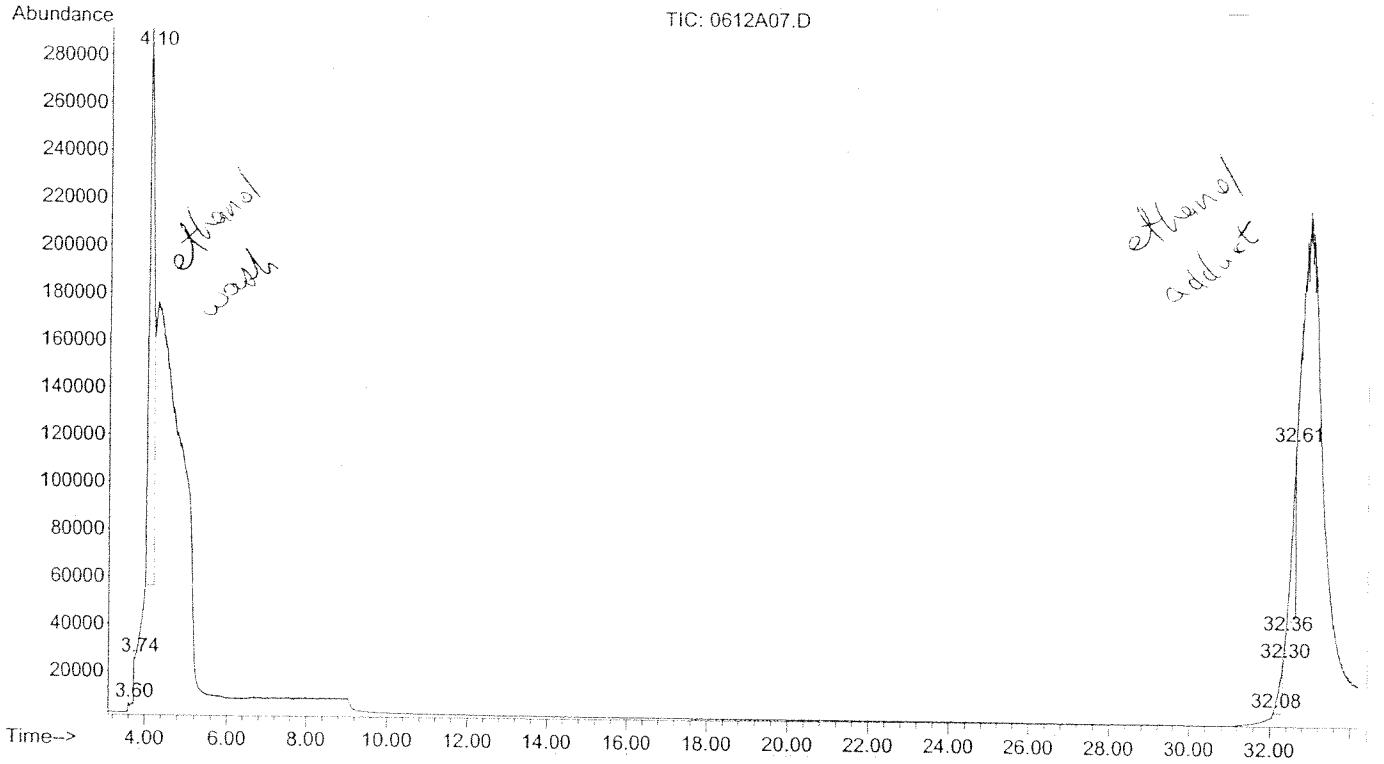
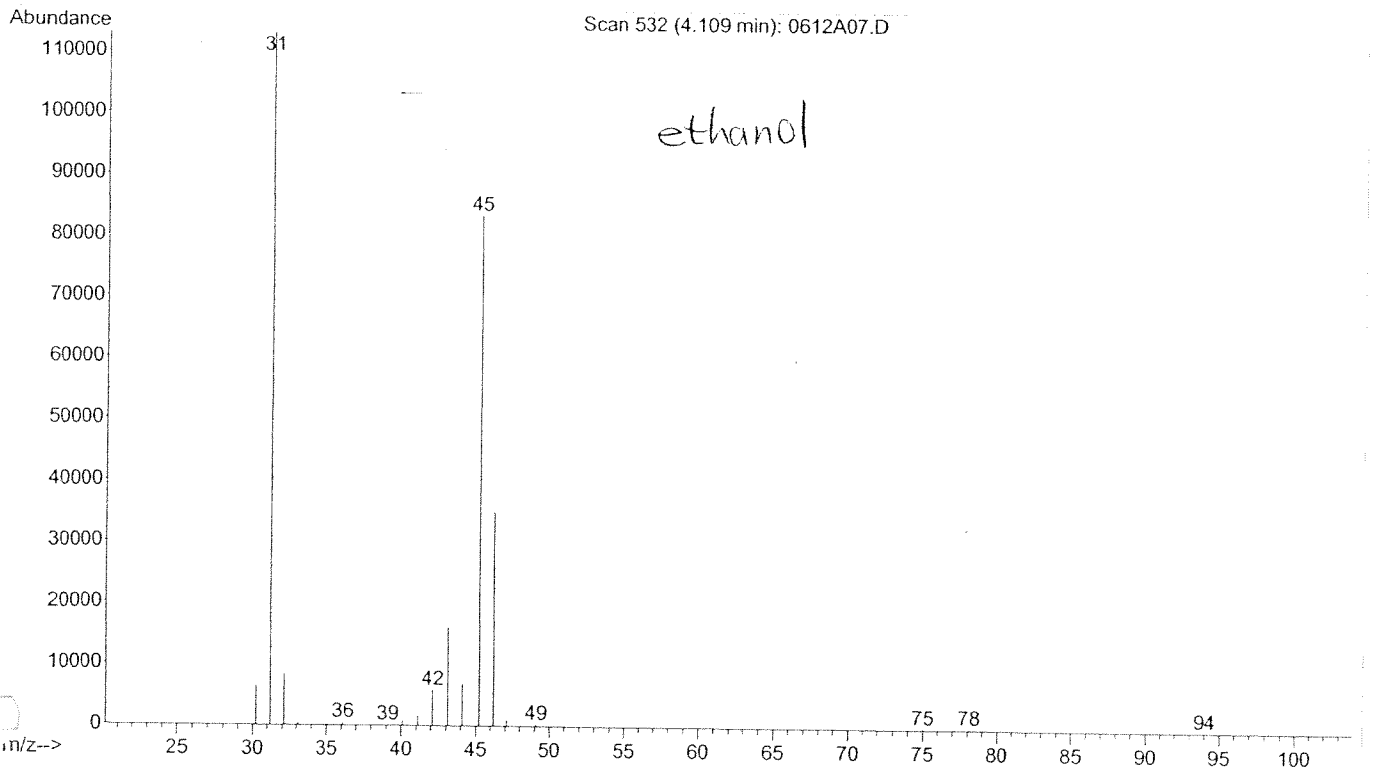
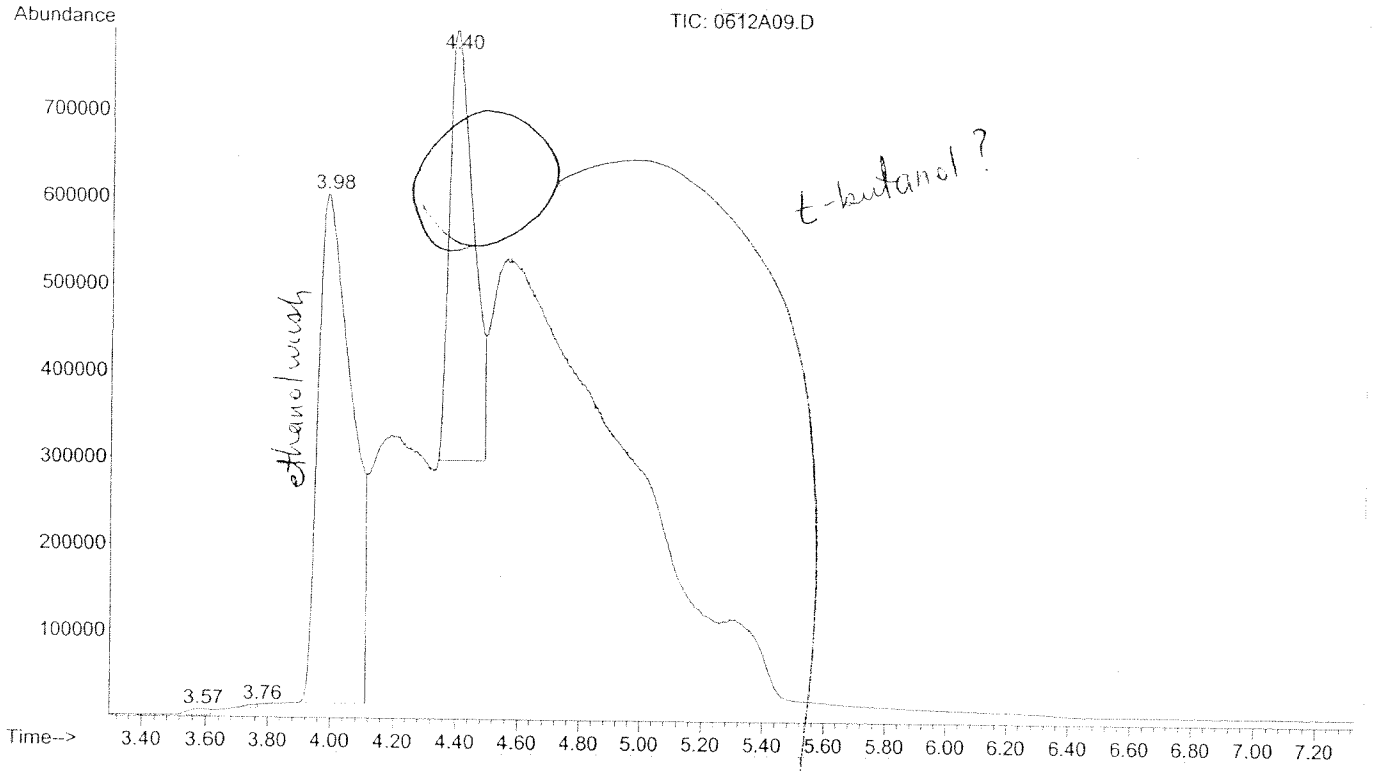
SLY 6-15-07

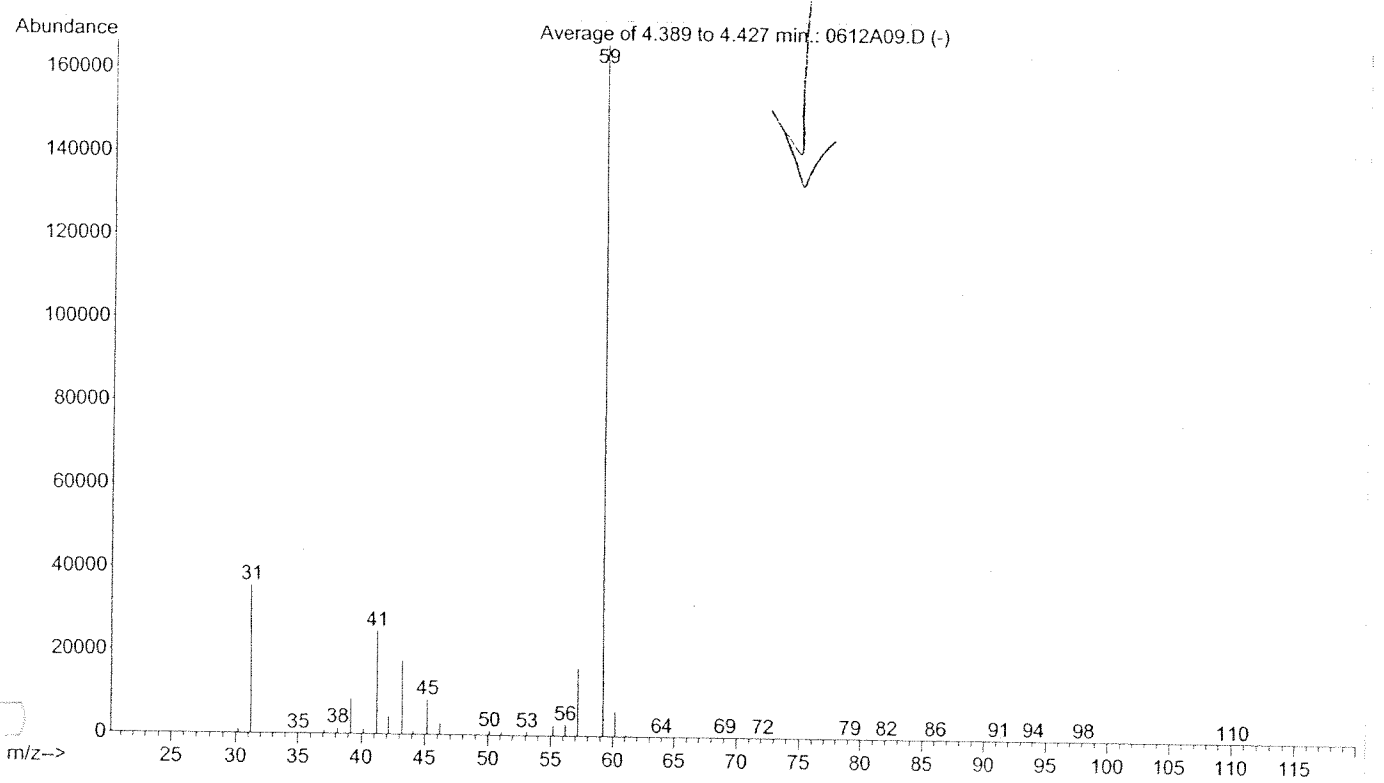




File : C:\MSDCHEM\1\DATA\OVI\0612A09.D
Operator : sly
Acquired : 13 Jun 2007 12:21 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 408376 alprostadil powder
Misc Info :
Vial Number: 6

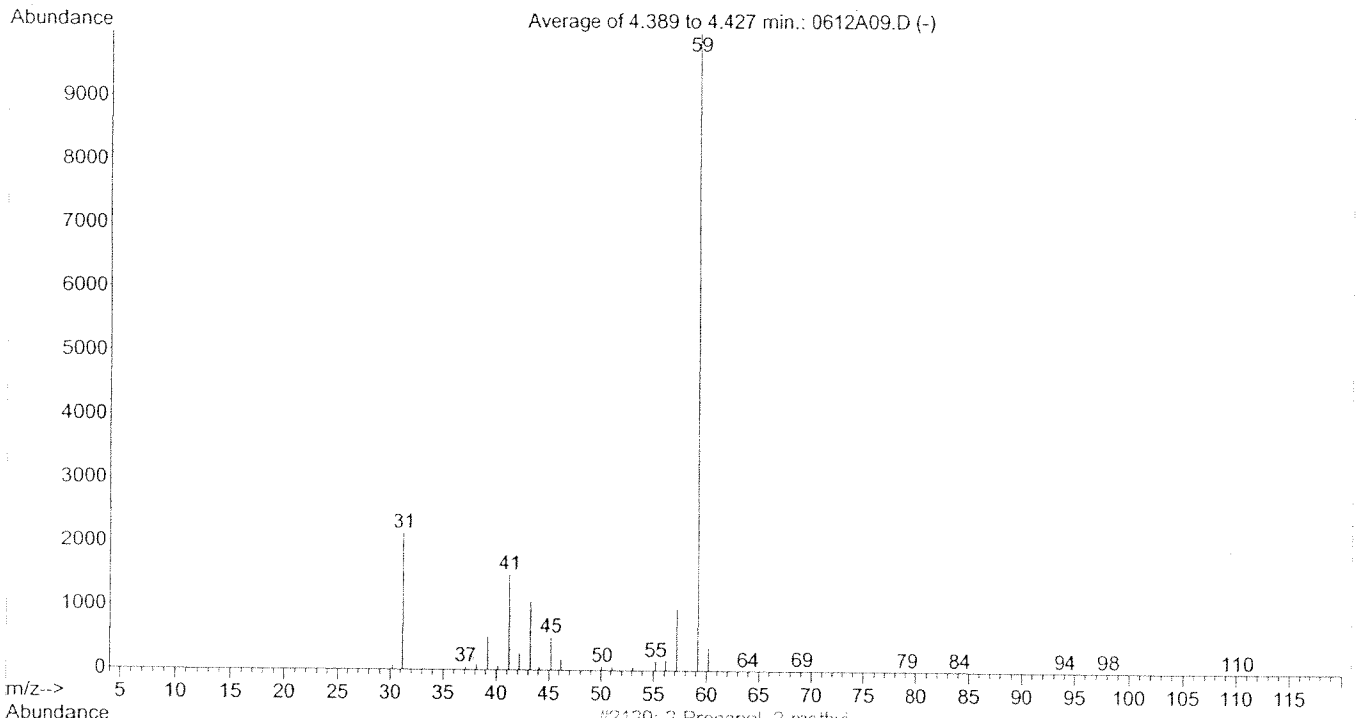
Sample # 377490
Attachment B pg 12 of 33
SLY 6-15-07

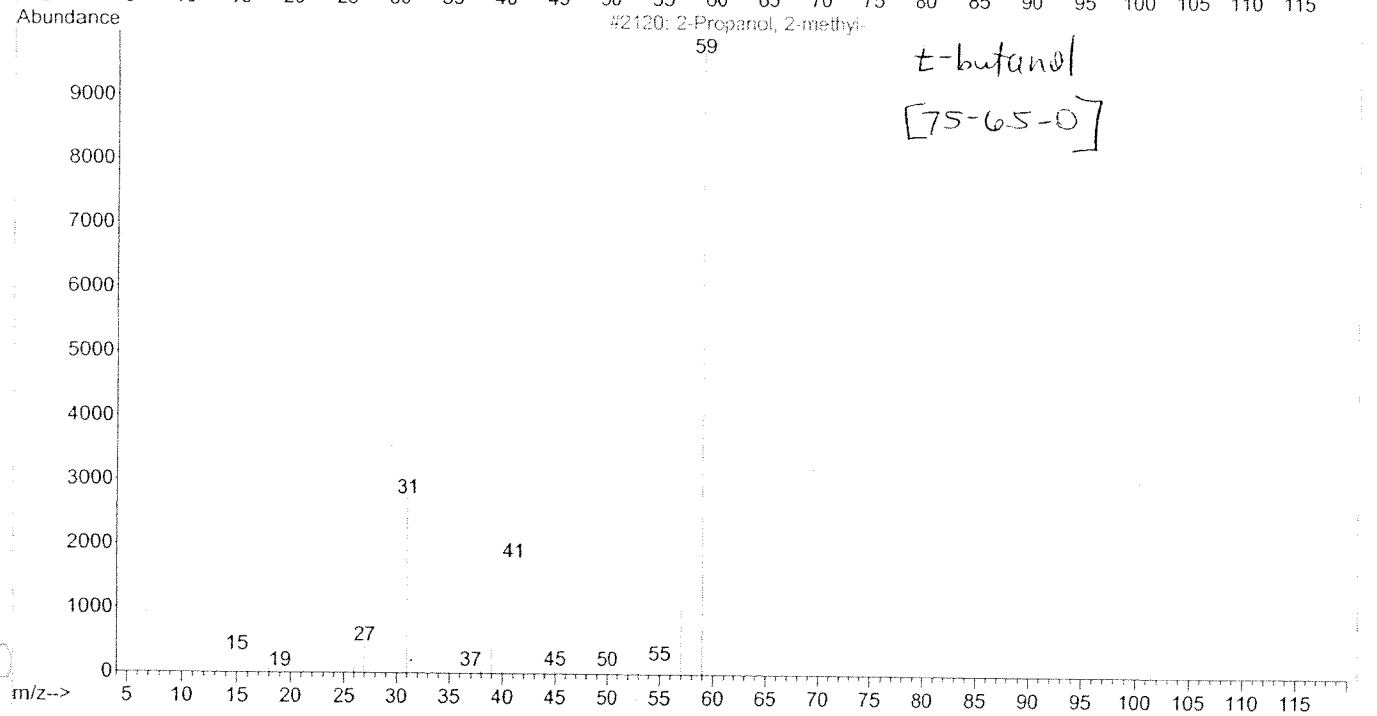




File : C:\MSDCHEM\1\DATA\OVI\0612A09.D
Operator : sly
Acquired : 13 Jun 2007 12:21 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 408376 alprostadil powder
Misc Info :
Vial Number: 6

Sample # 377410
Attachment 8 pg 13 of 33
SLY
6-15-07





t-butanol
[75-65-0]

File : C:\MSDCHEM\1\DATA\OVI\0612A11.D
Operator : sly
Acquired : 13 Jun 2007 13:22 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 414717 alprostadil liquid
Misc Info :
Vial Number: 7

Sample # 37740
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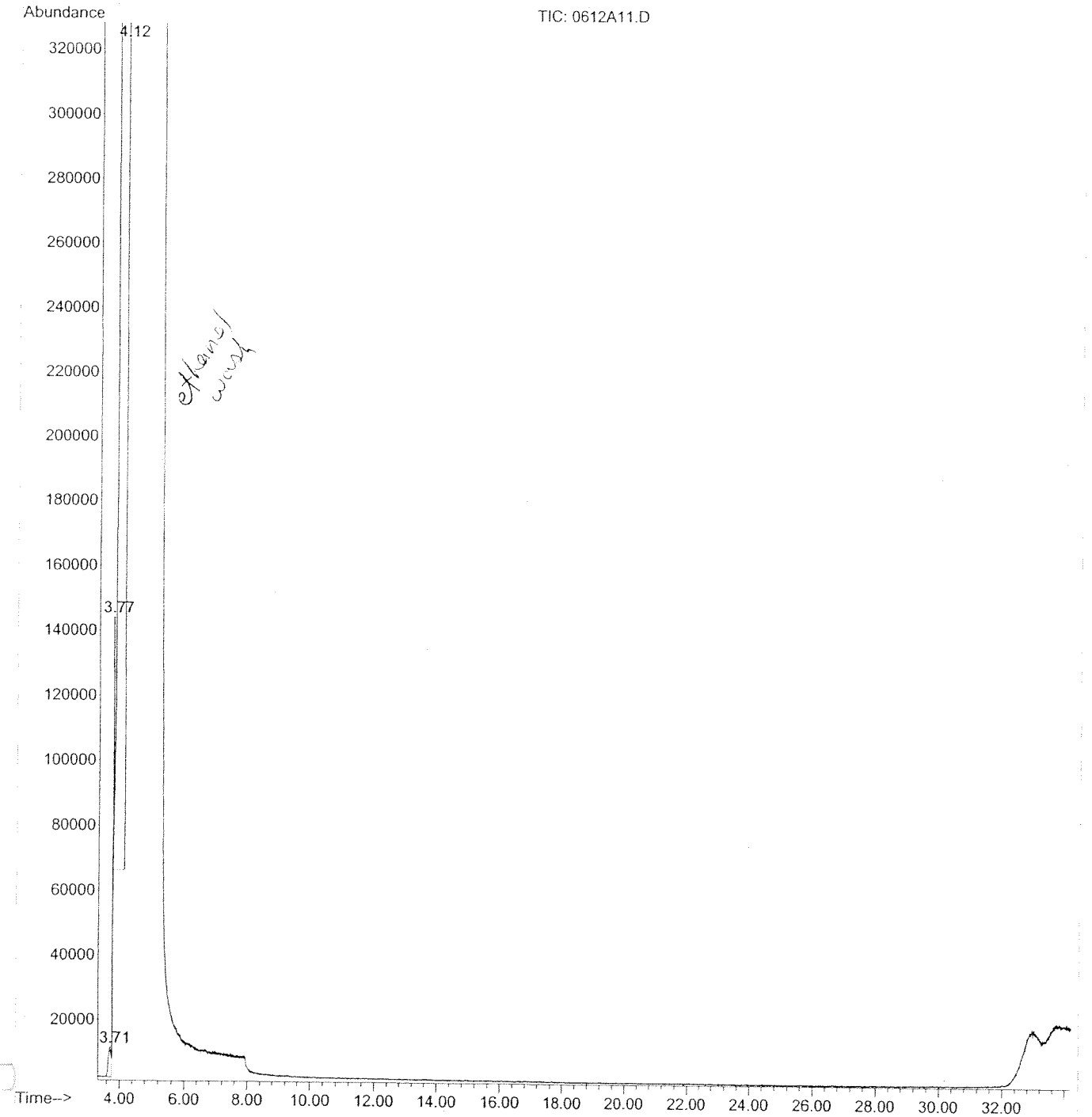

File : C:\MSDCHEM\1\DATA\OVI\0612A13.D
Operator : sly
Acquired : 13 Jun 2007 14:23 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 420529 alprostadil liquid
Misc Info :
Vial Number: 8

Sample # 37740
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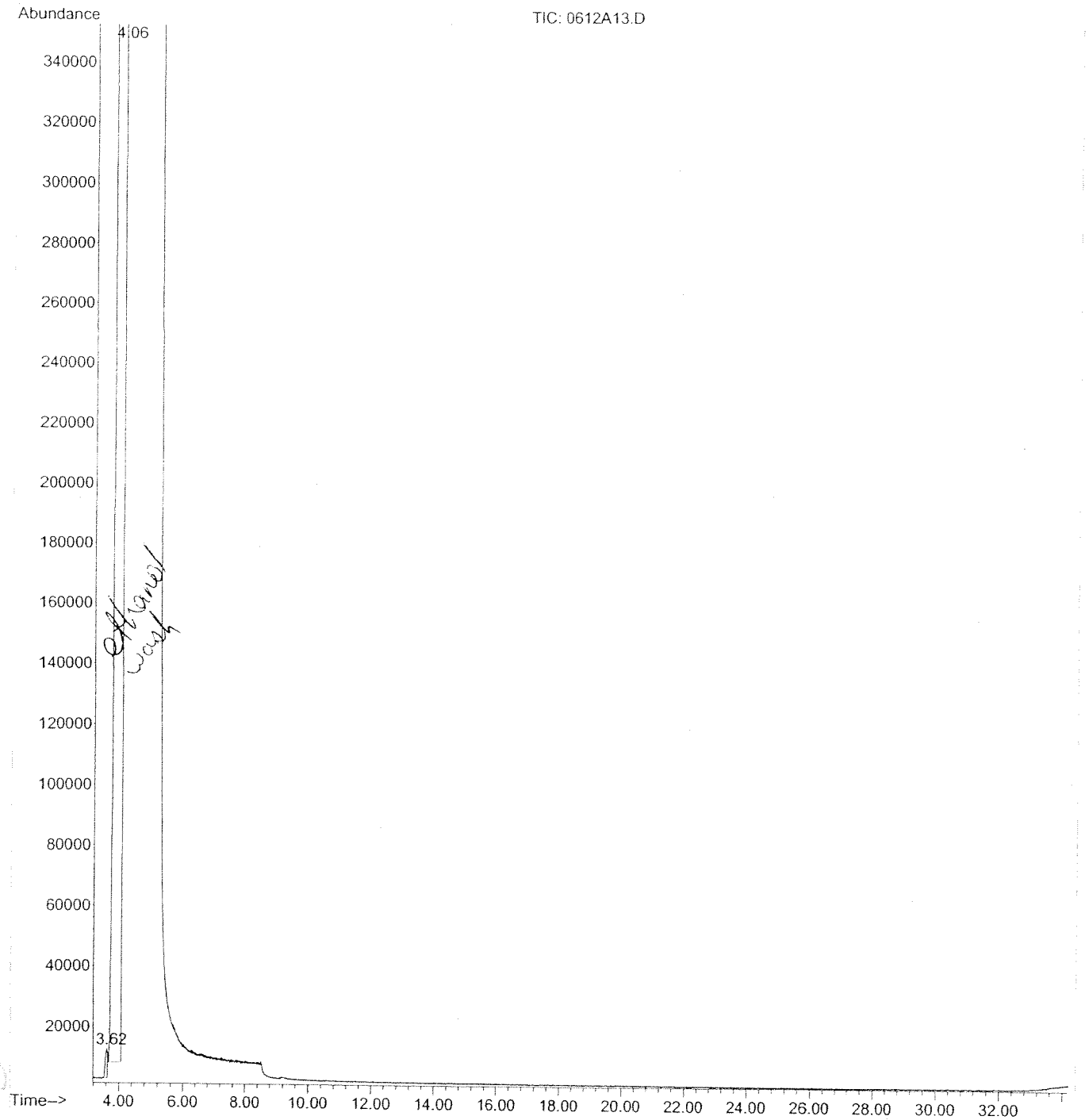

File : C:\MSDCHEM\1\DATA\OVI\0612A15.D
Operator : sly
Acquired : 13 Jun 2007 15:24 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 412621 codeine
Misc Info :
Vial Number: 9

Sample # 377410
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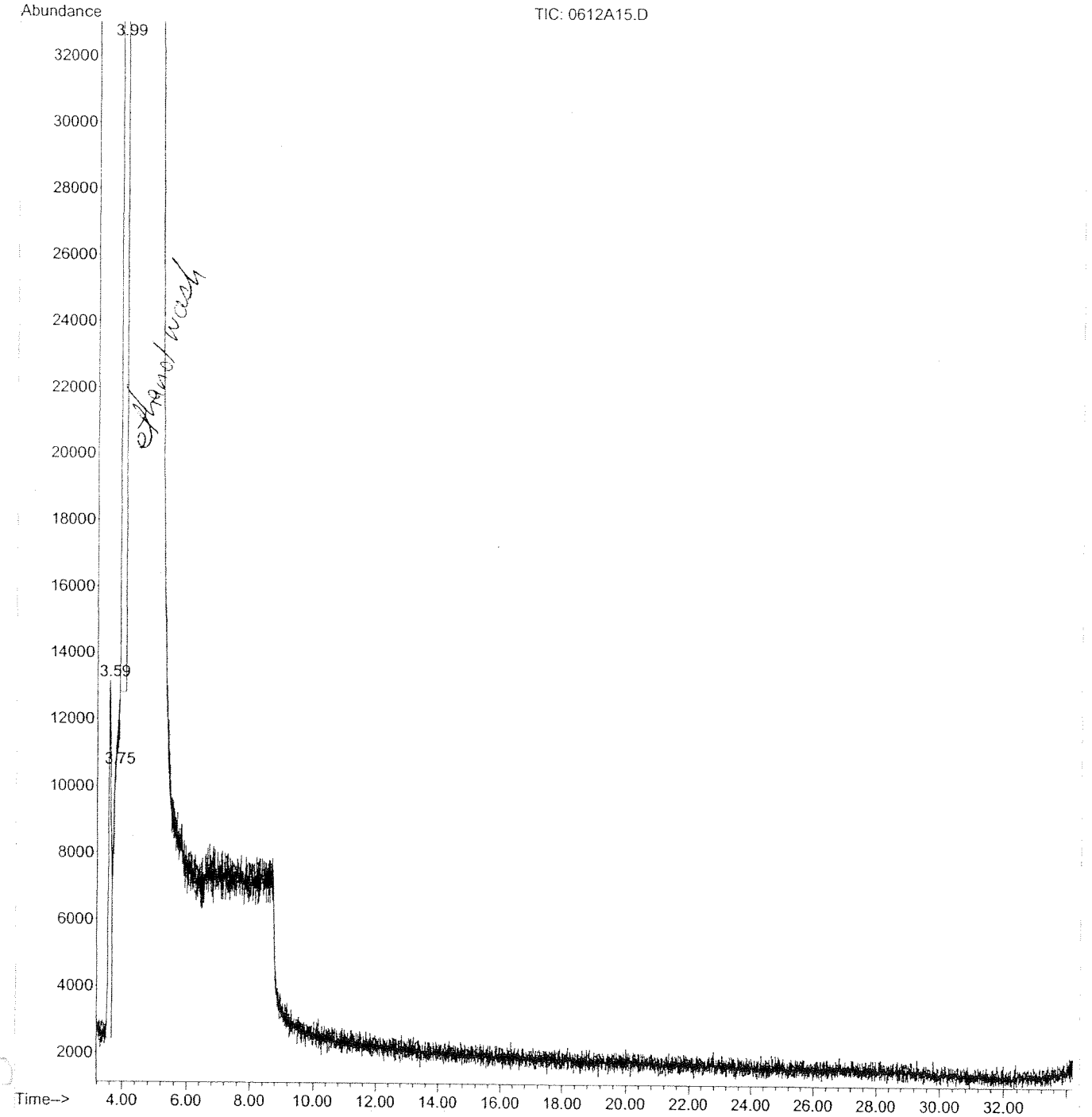

File : C:\MSDCHEM\1\DATA\OVI\0612A17.D
Operator : sly
Acquired : 13 Jun 2007 16:24 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS1
Misc Info :
Vial Number: 3

Sample # 377419
Attachment B pg 17 of 33
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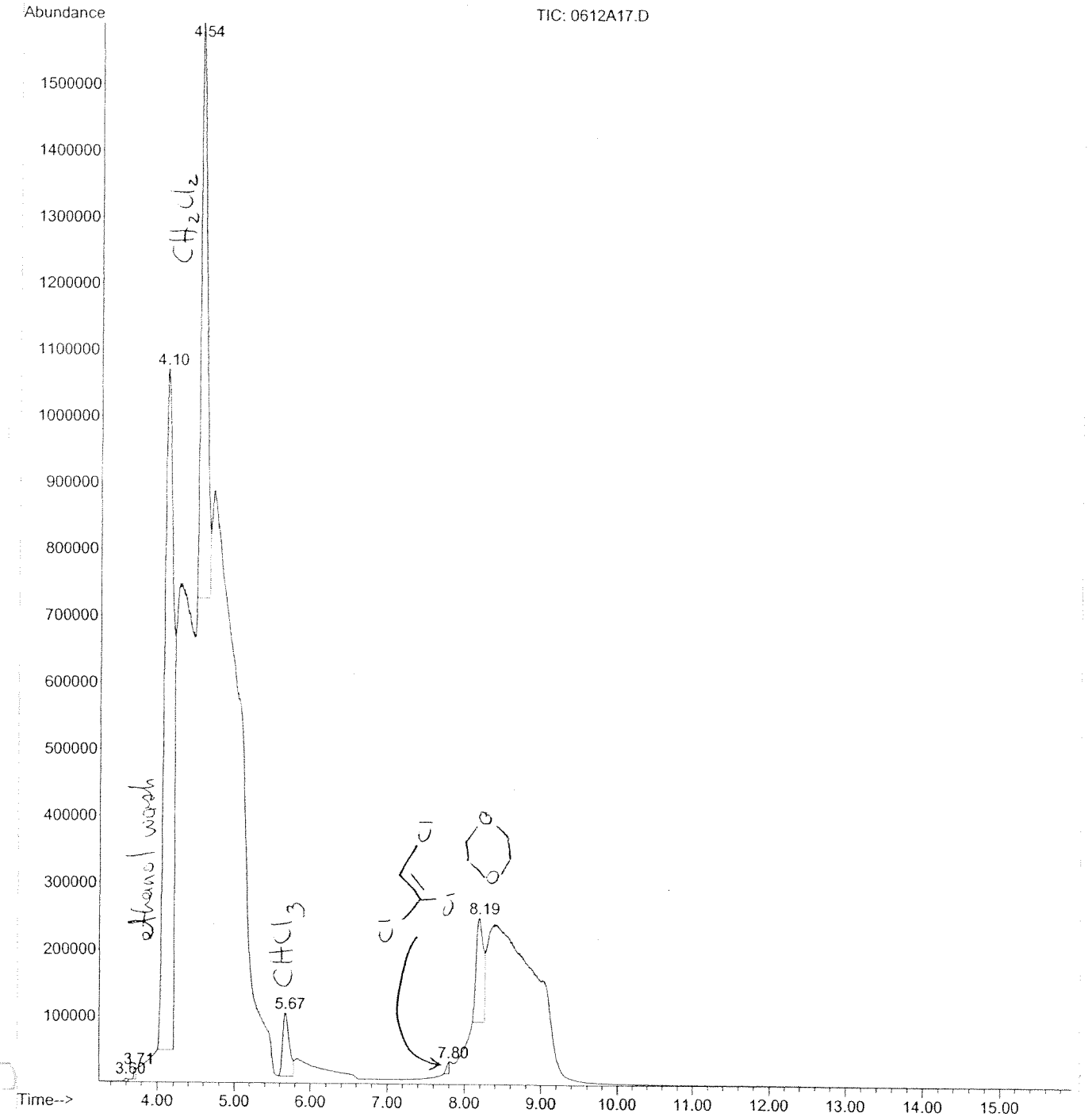

File : C:\MSDCHEM\1\DATA\OVI\0612A19.D
Operator : sly
Acquired : 13 Jun 2007 17:25 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 420501 nefazod
Misc Info :
Vial Number: 10

Sample # 377410
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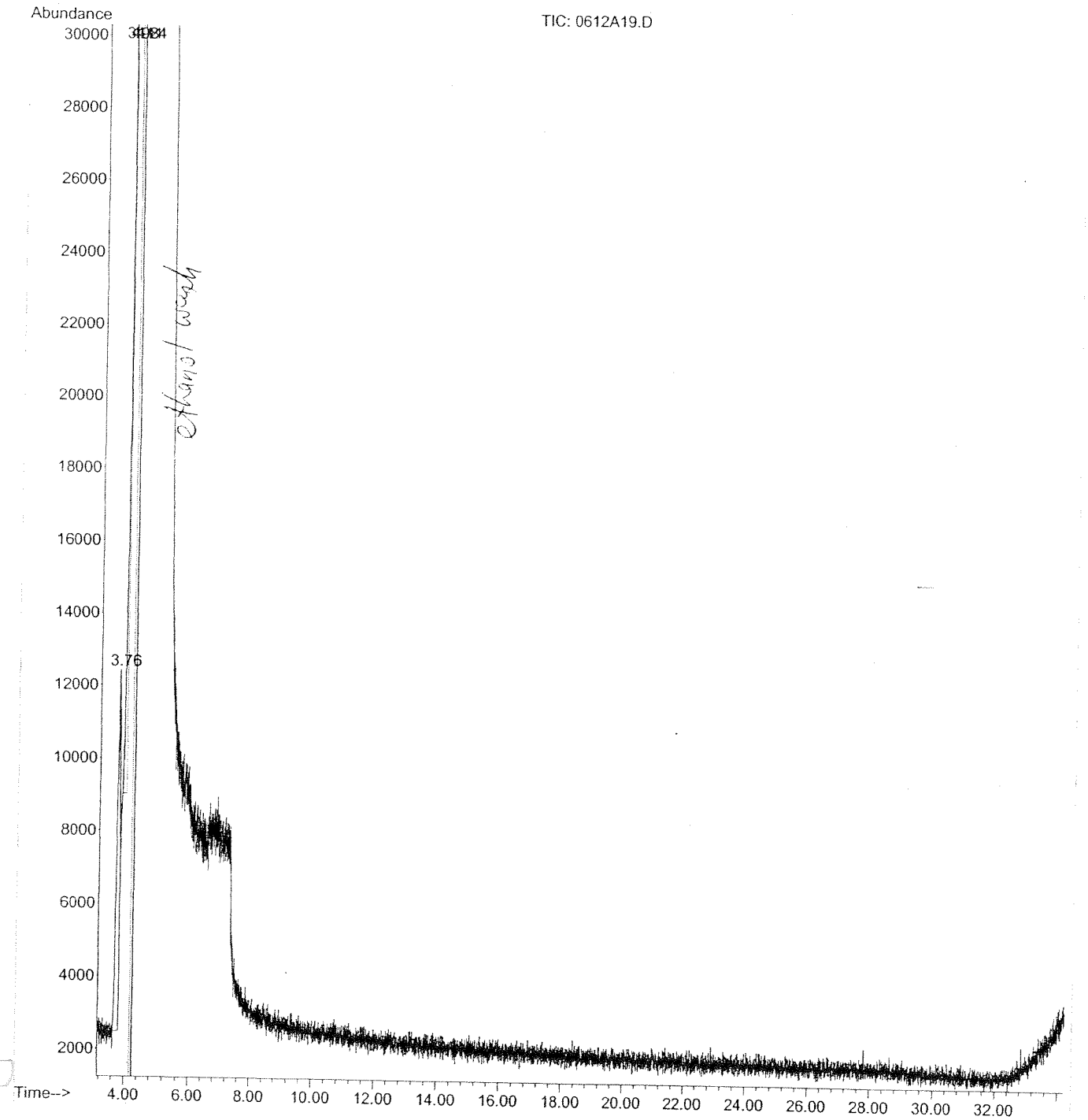

File : C:\MSDCHEM\1\DATA\OVI\0612A21.D
Operator : sly
Acquired : 13 Jun 2007 18:25 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 383890 naproxen
Misc Info :
Vial Number: 11

Sample # 377410
Attachment B pg 19 of 33
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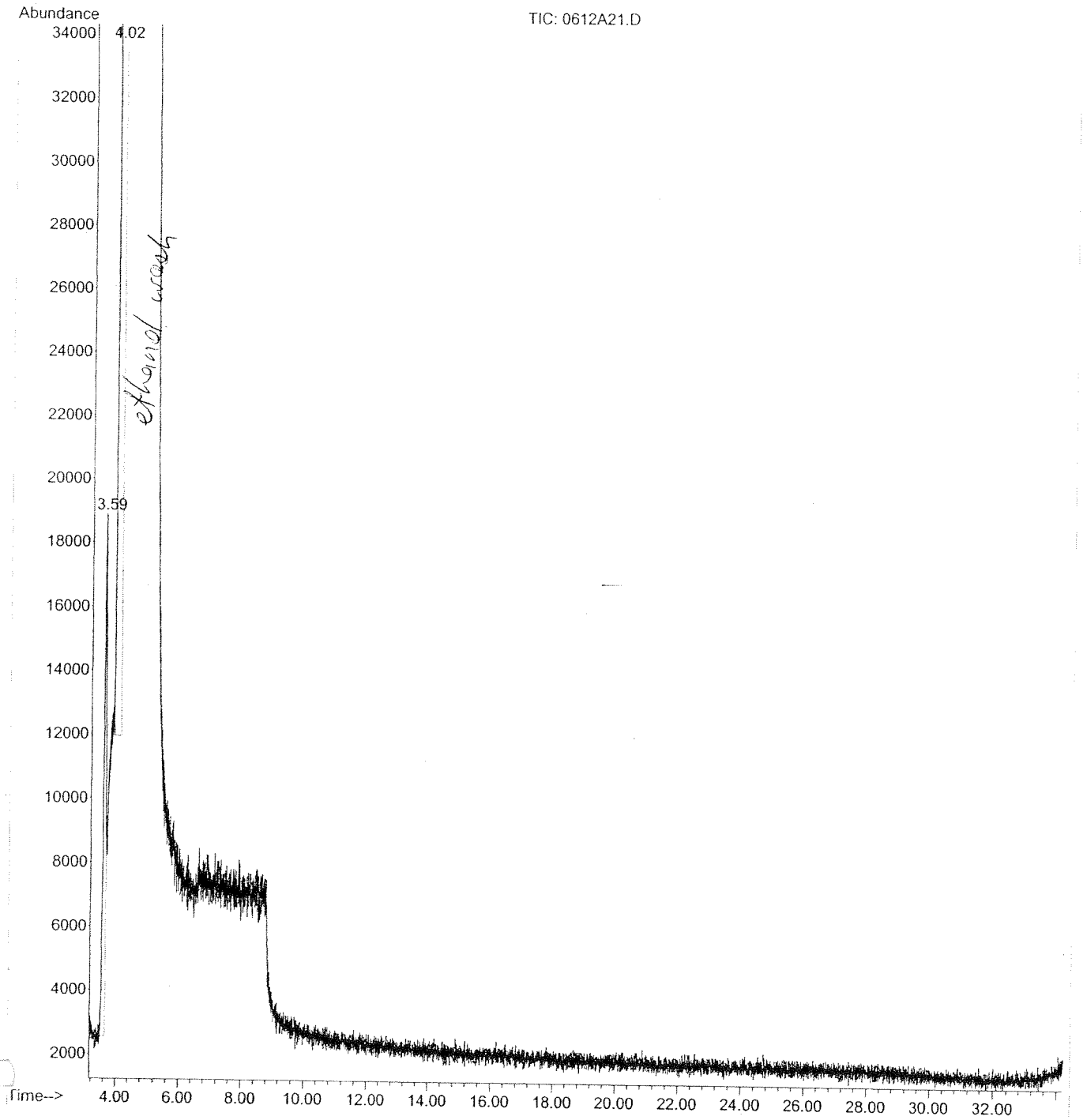

File : C:\MSDCHEM\1\DATA\OVI\0612A23.D
Operator : sly
Acquired : 13 Jun 2007 19:27 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 383890 spike 1
Misc Info :
Vial Number: 12

Sample # 377410
Attachment 10 pg 20 of 33
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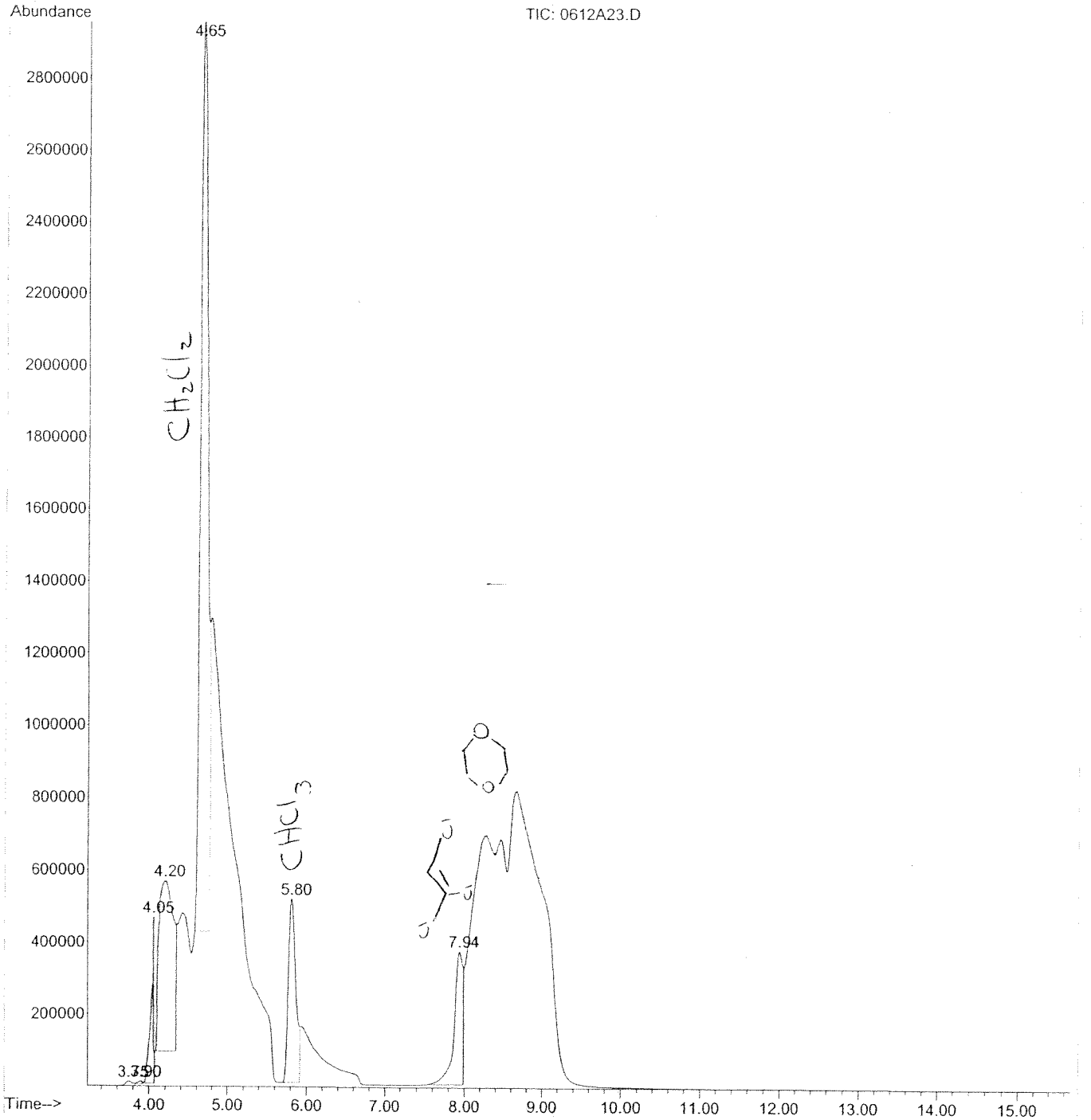

File : C:\MSDCHEM\1\DATA\OVI\0612A25.D
Operator : sly
Acquired : 13 Jun 2007 20:27 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 383891 naproxen
Misc Info :
Vial Number: 13

Sample # 377410
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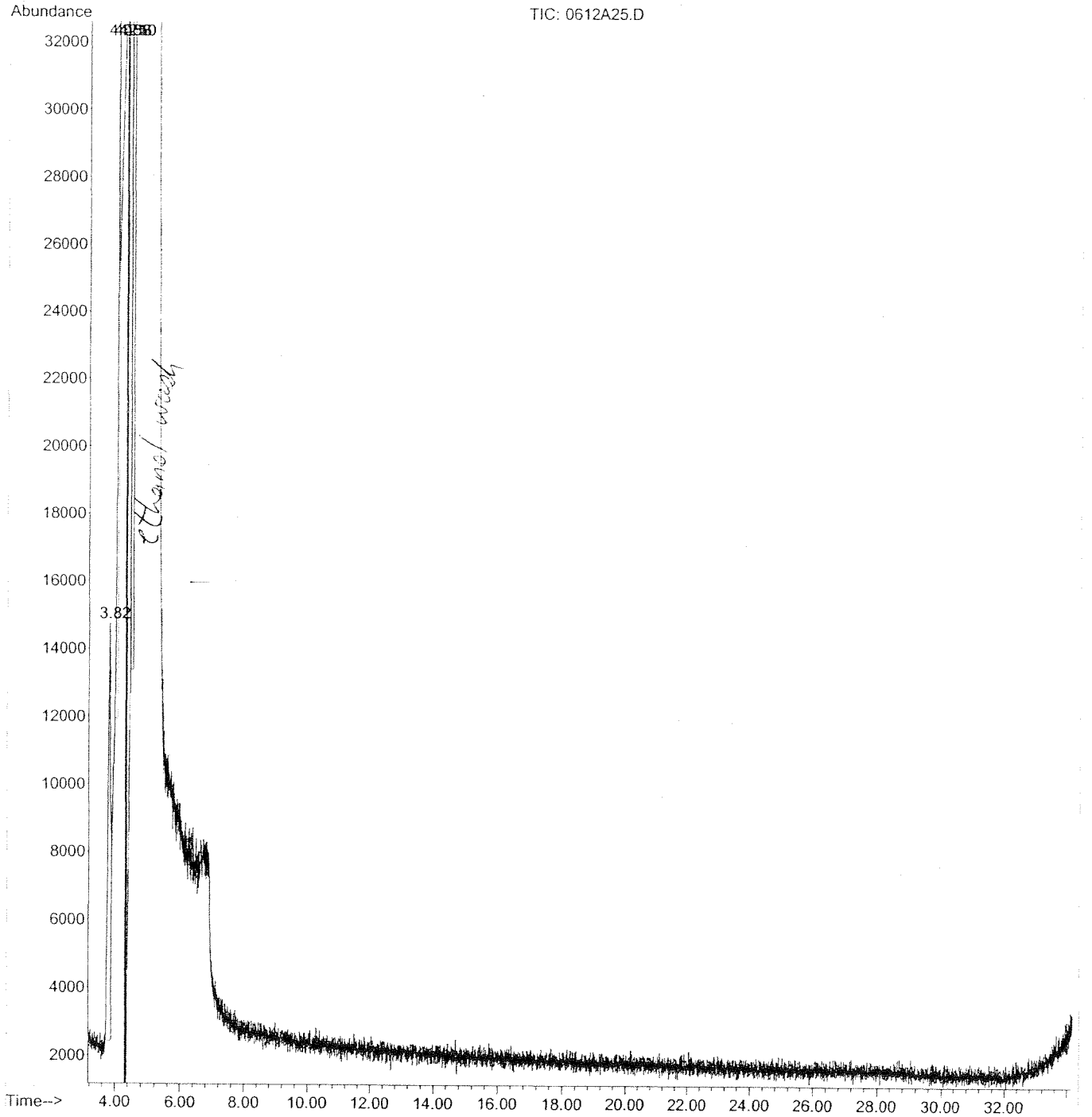
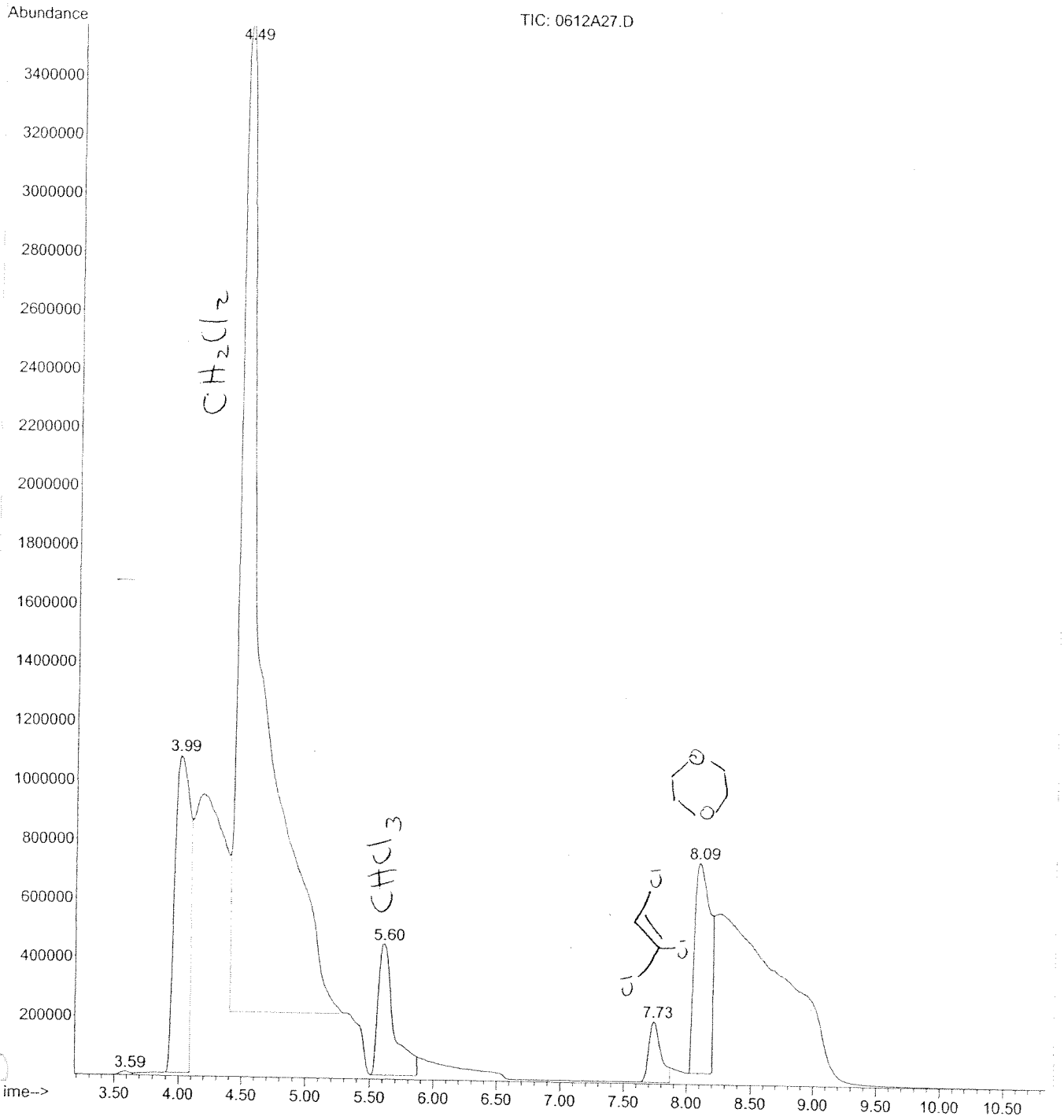


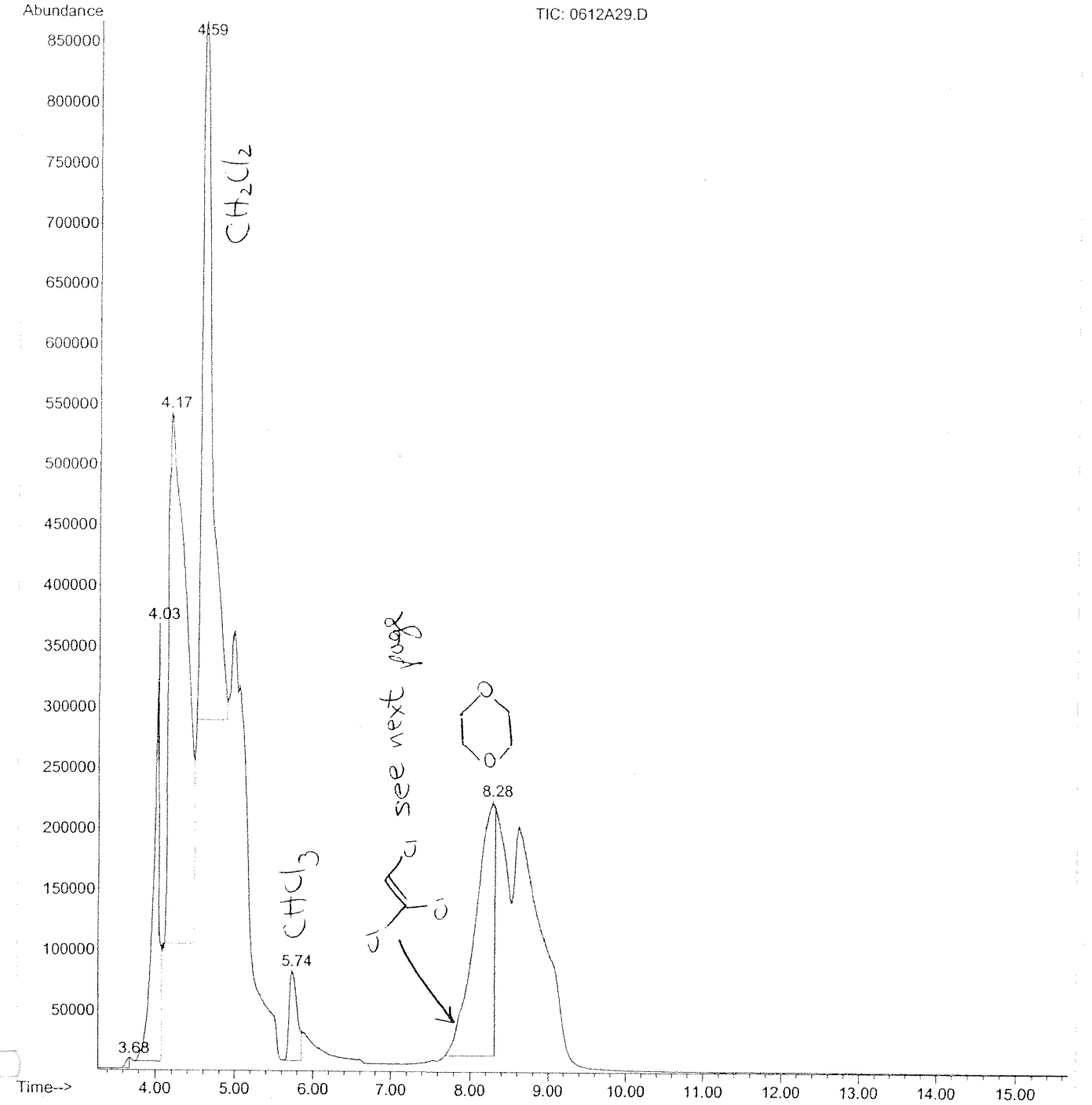
File : C:\MSDCHEM\1\DATA\OVI\0612A27.D
Operator : sly
Acquired : 13 Jun 2007 21:28 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 383891 spike 2
Misc Info :
Vial Number: 14

Sample # 377410
Attachment B pg 22 of 33
SLY 6-15-07



File : C:\MSDCHEM\1\DATA\OVI\0612A29.D
Operator : sly
Acquired : 13 Jun 2007 22:30 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS1
Misc Info :
Vial Number: 3

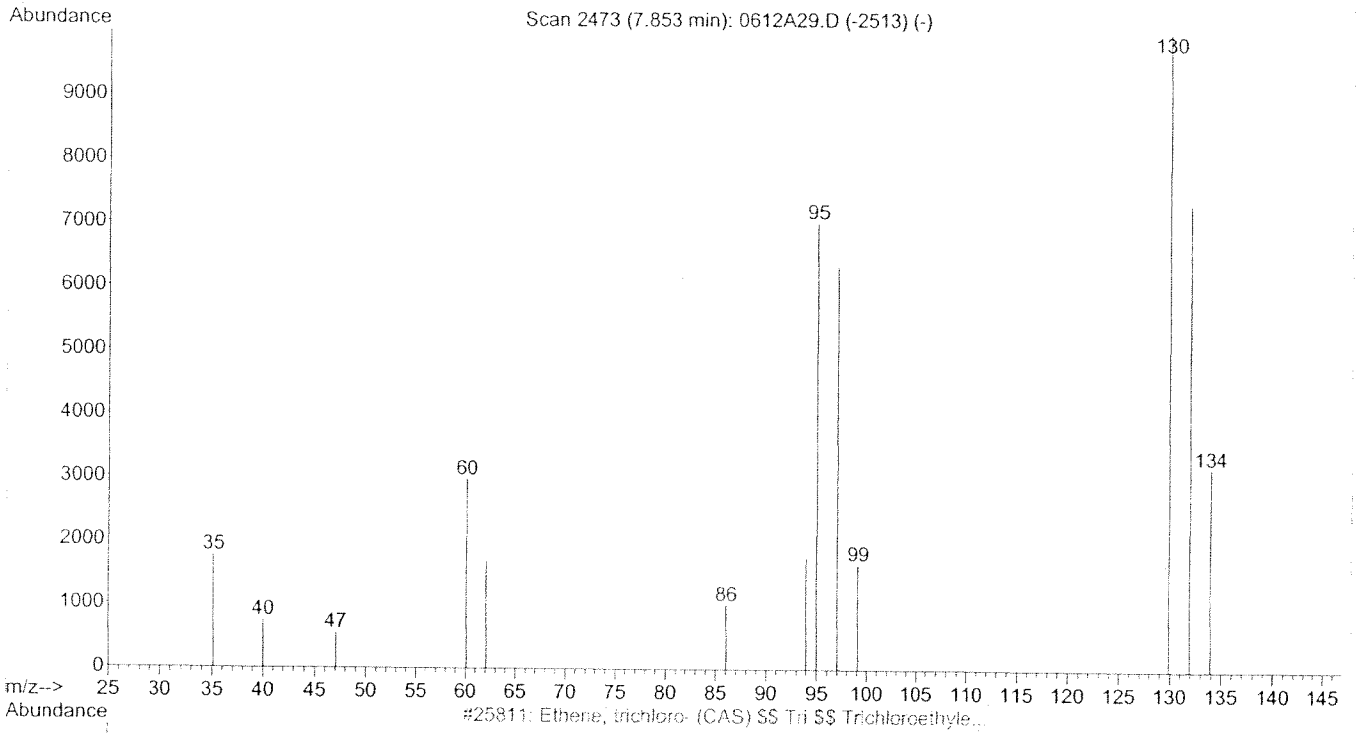
Sample # 377410
Attachment B pg 23 of 33
SLY 6-15-07

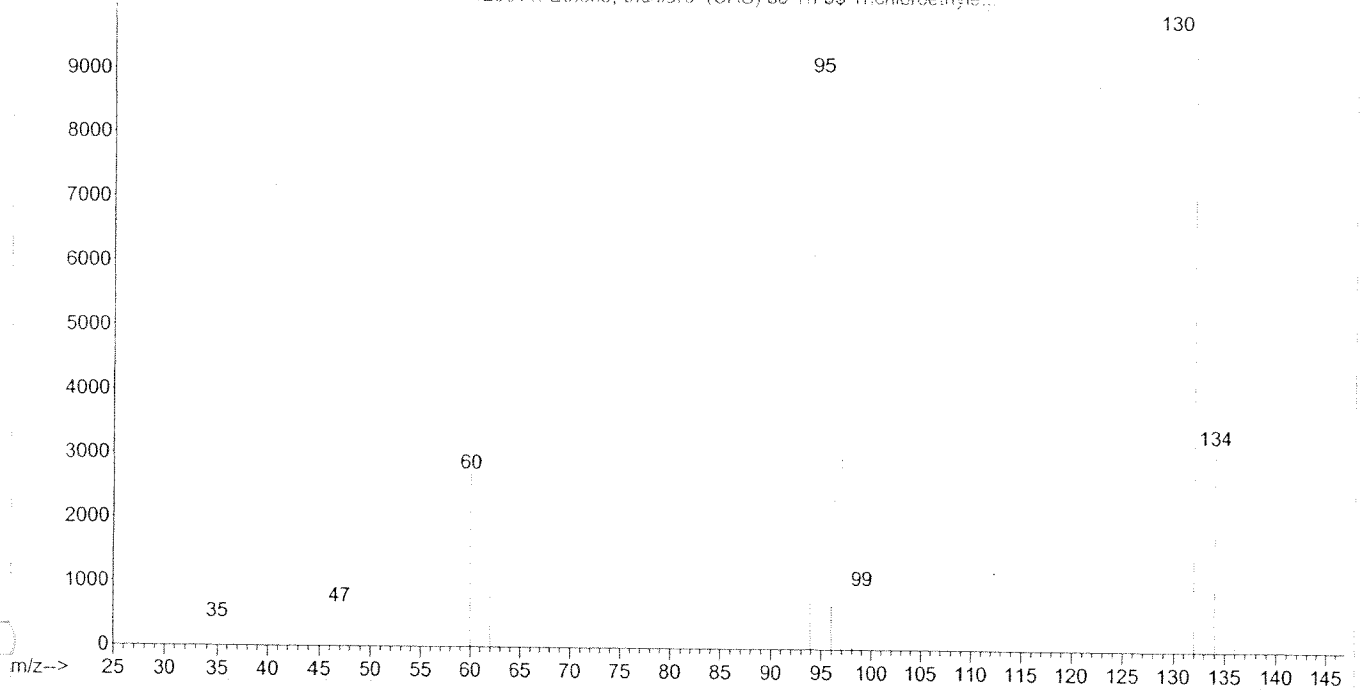


File : C:\MSDCHEM\1\DATA\OVI\0612A29.D
Operator : sly
Acquired : 13 Jun 2007 22:30 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS1
Misc Info :
Vial Number: 3

Trichloroethylene

Sample # 377410
Attachment B pg 24 of 30
SLY
6-15-07





File : C:\MSDCHEM\1\DATA\OVI\0612A31.D
Operator : sly
Acquired : 13 Jun 2007 23:31 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 408372 naproxen
Misc Info :
Vial Number: 15

Sample # 377410
Attachment B pg 25 of 33
SLY
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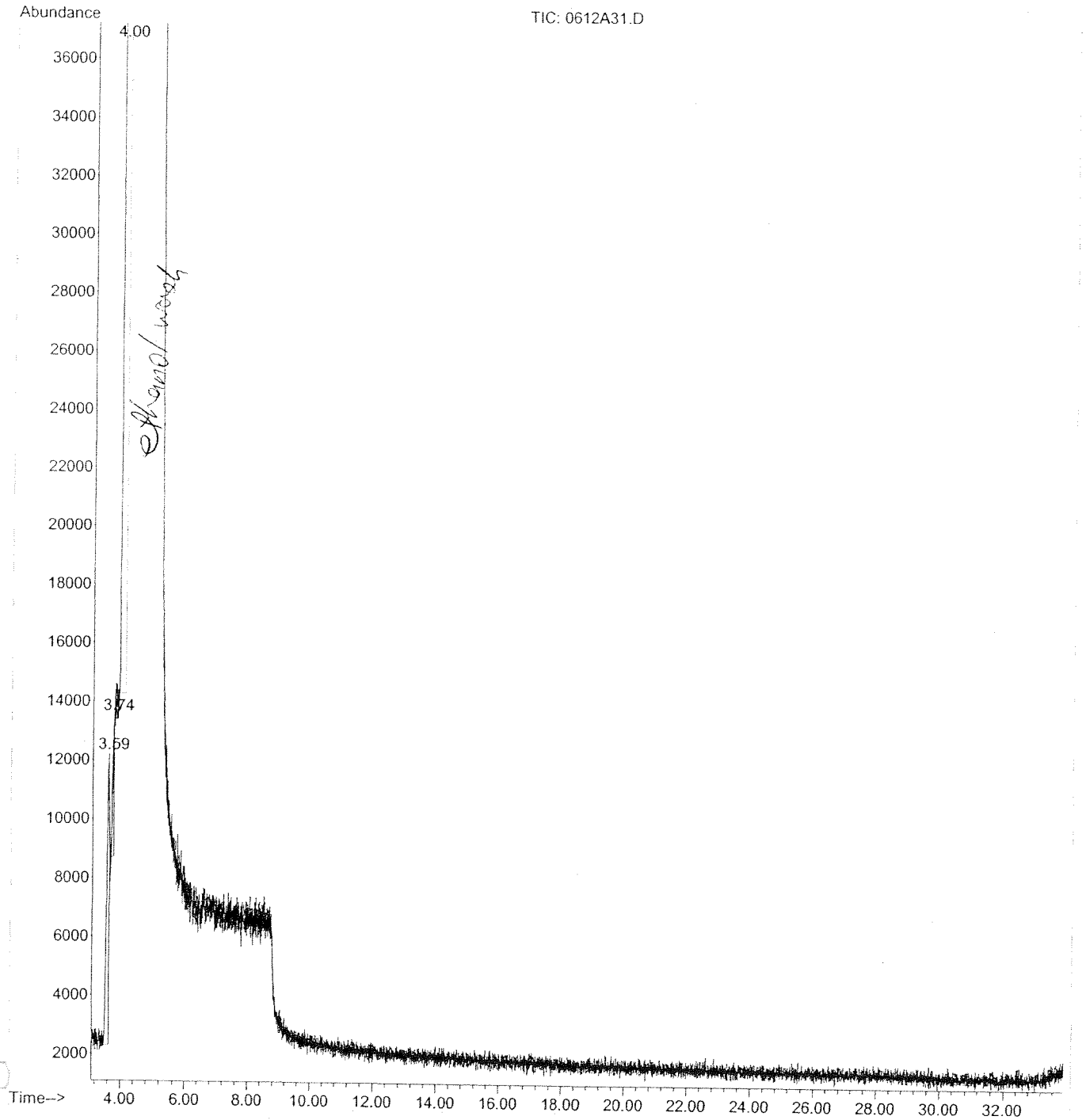

File : C:\MSDCHEM\1\DATA\OVI\0612A33.D
Operator : sly
Acquired : 14 Jun 2007 00:32 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 409673 naproxen
Misc Info :
Vial Number: 16

Sample # 377410
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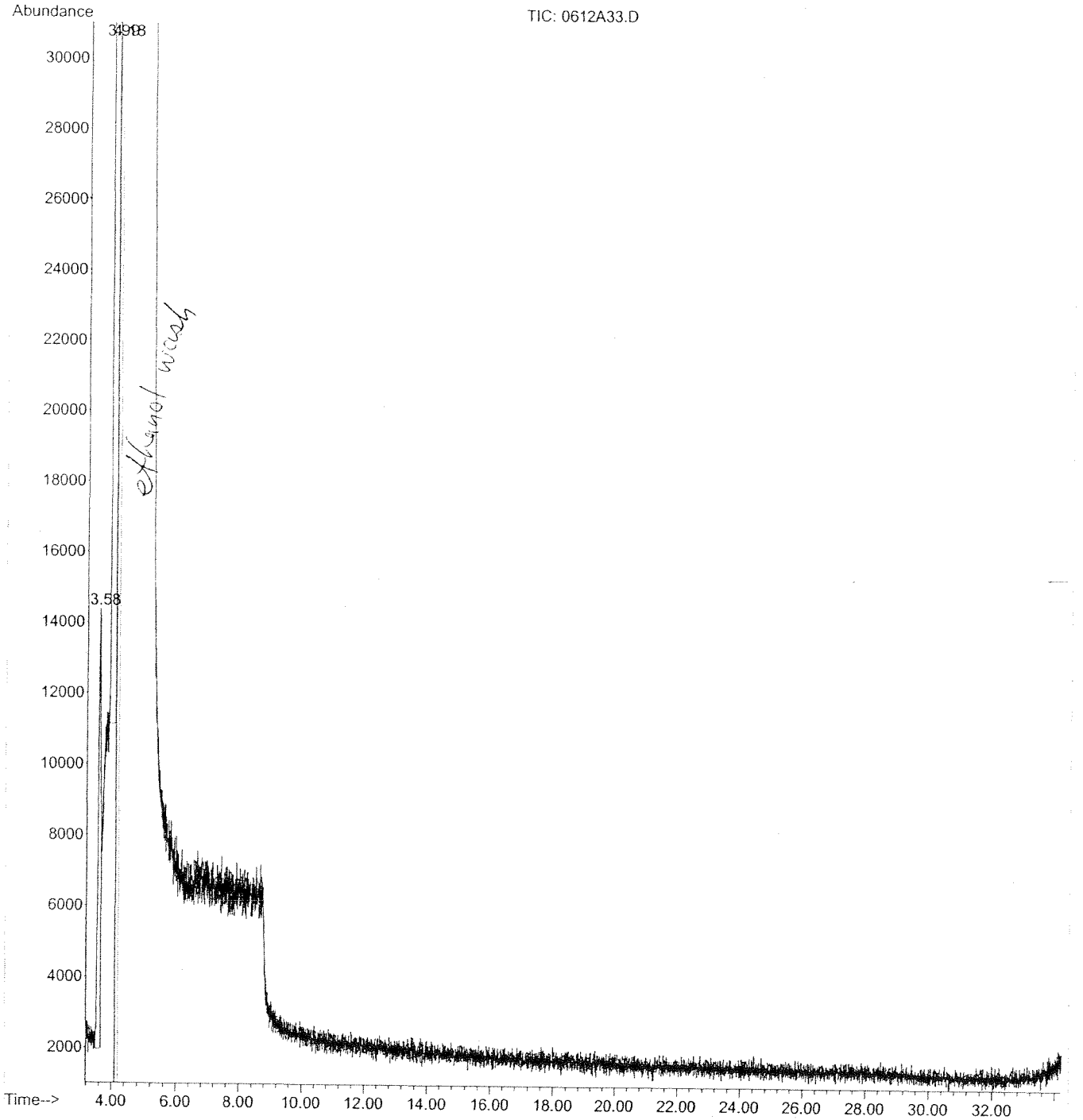

File : C:\MSDCHEM\1\DATA\OVI\0612A35.D
Operator : sly
Acquired : 14 Jun 2007 1:33 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 409674 naproxen
Misc Info :
Vial Number: 17

Sample # 377416
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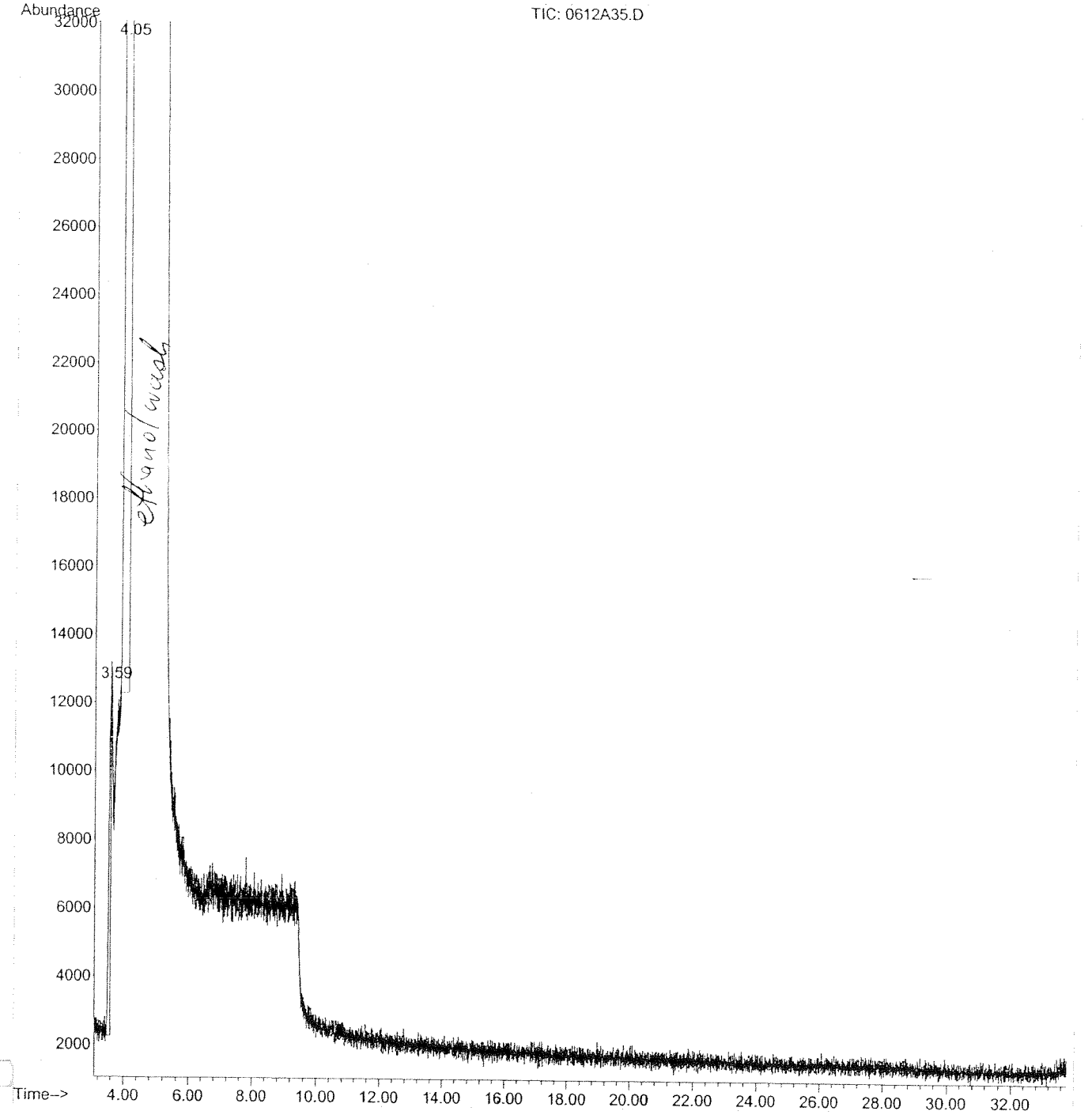
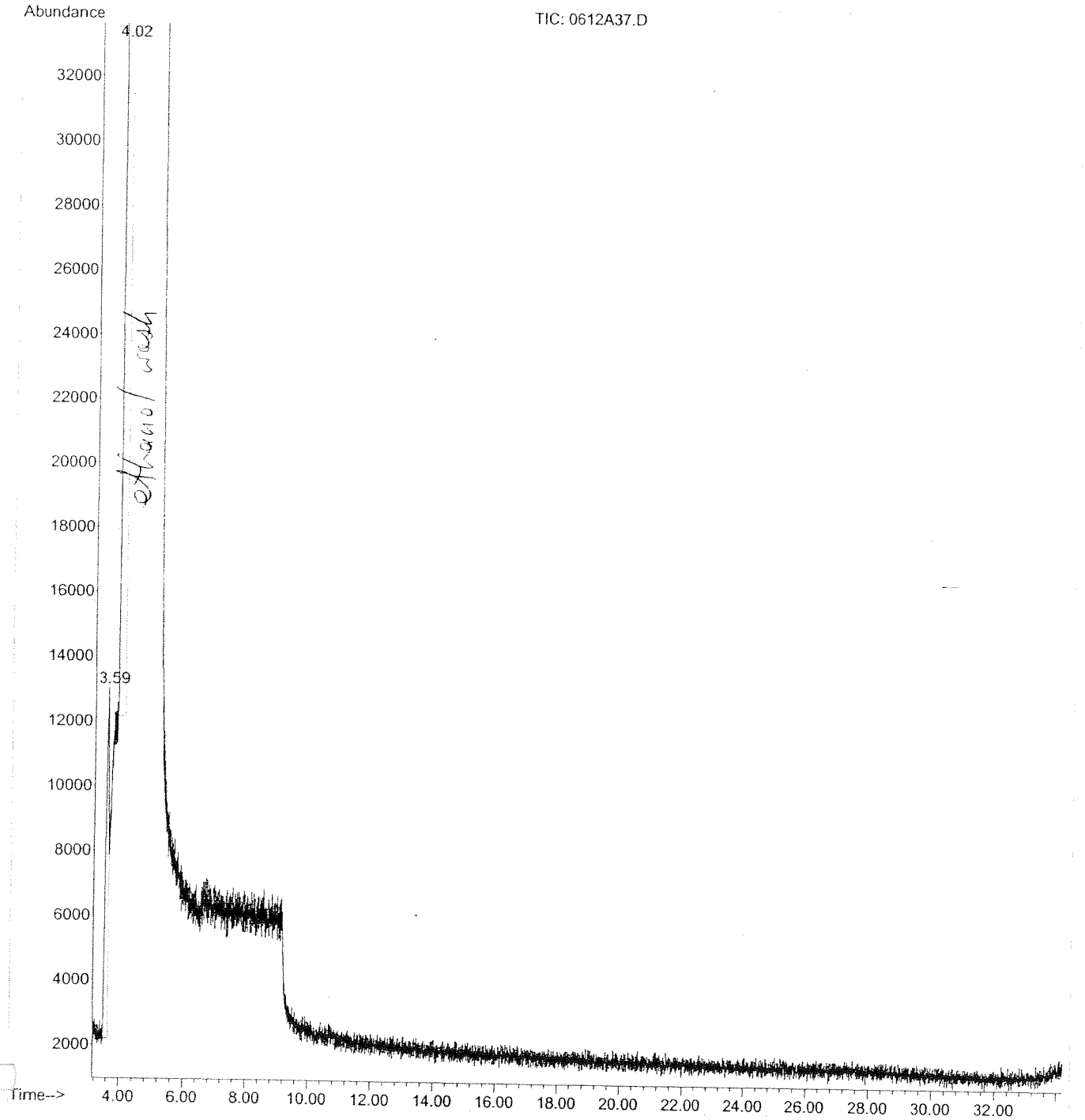
SLY
6-15-07



File : C:\MSDCHEM\1\DATA\OVI\0612A37.D
Operator : sly
Acquired : 14 Jun 2007 2:34 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 423339 naproxen
Misc Info :
Vial Number: 18

Sample # 377410
Attachment 8 pg 28 of 33
SLY
6-15-07



File : C:\MSDCHEM\1\DATA\OVI\0612A39.D
Operator : sly
Acquired : 14 Jun 2007 3:36 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 423340 naproxen
Misc Info :
Vial Number: 19

Sample # 377410
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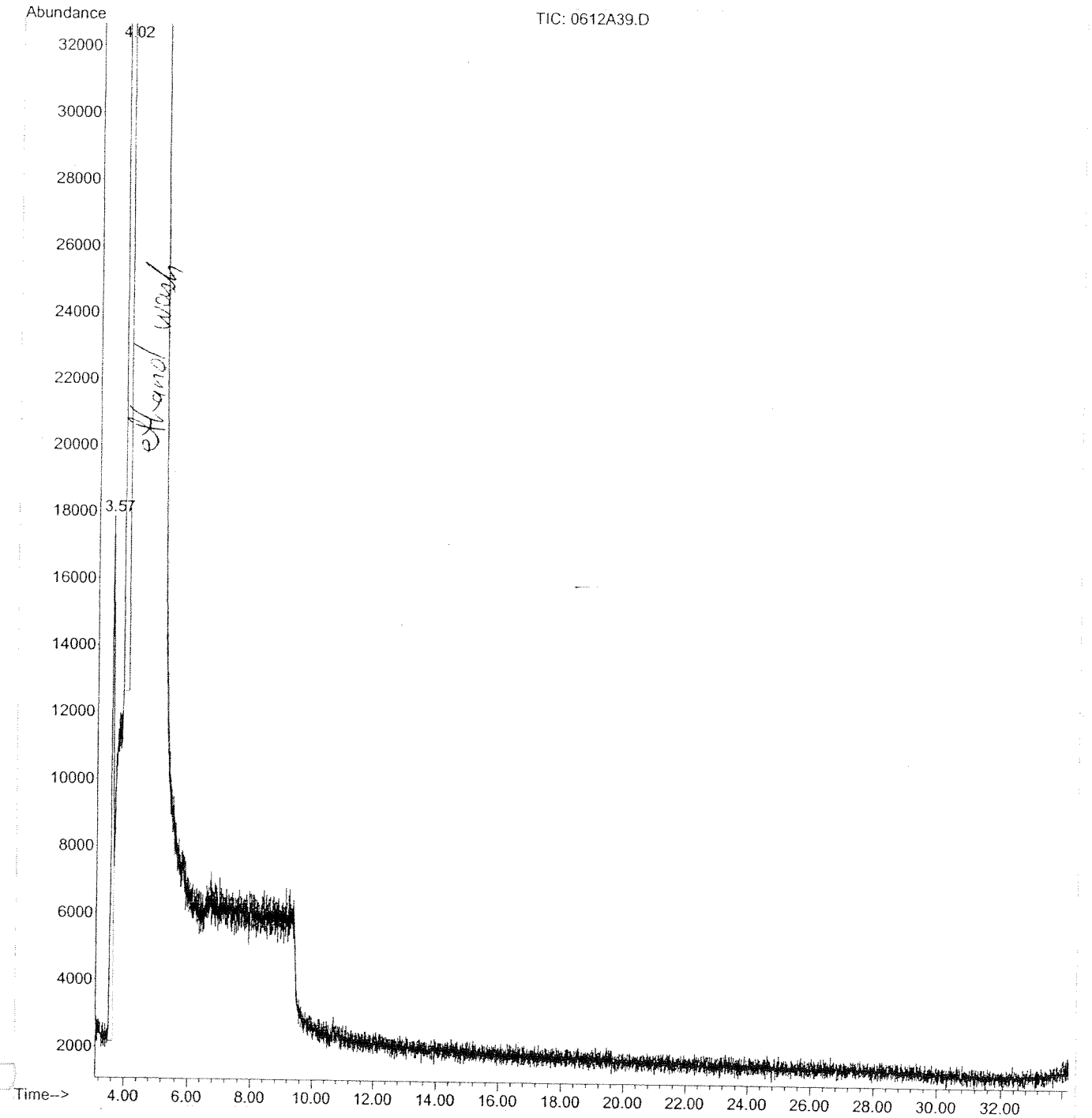
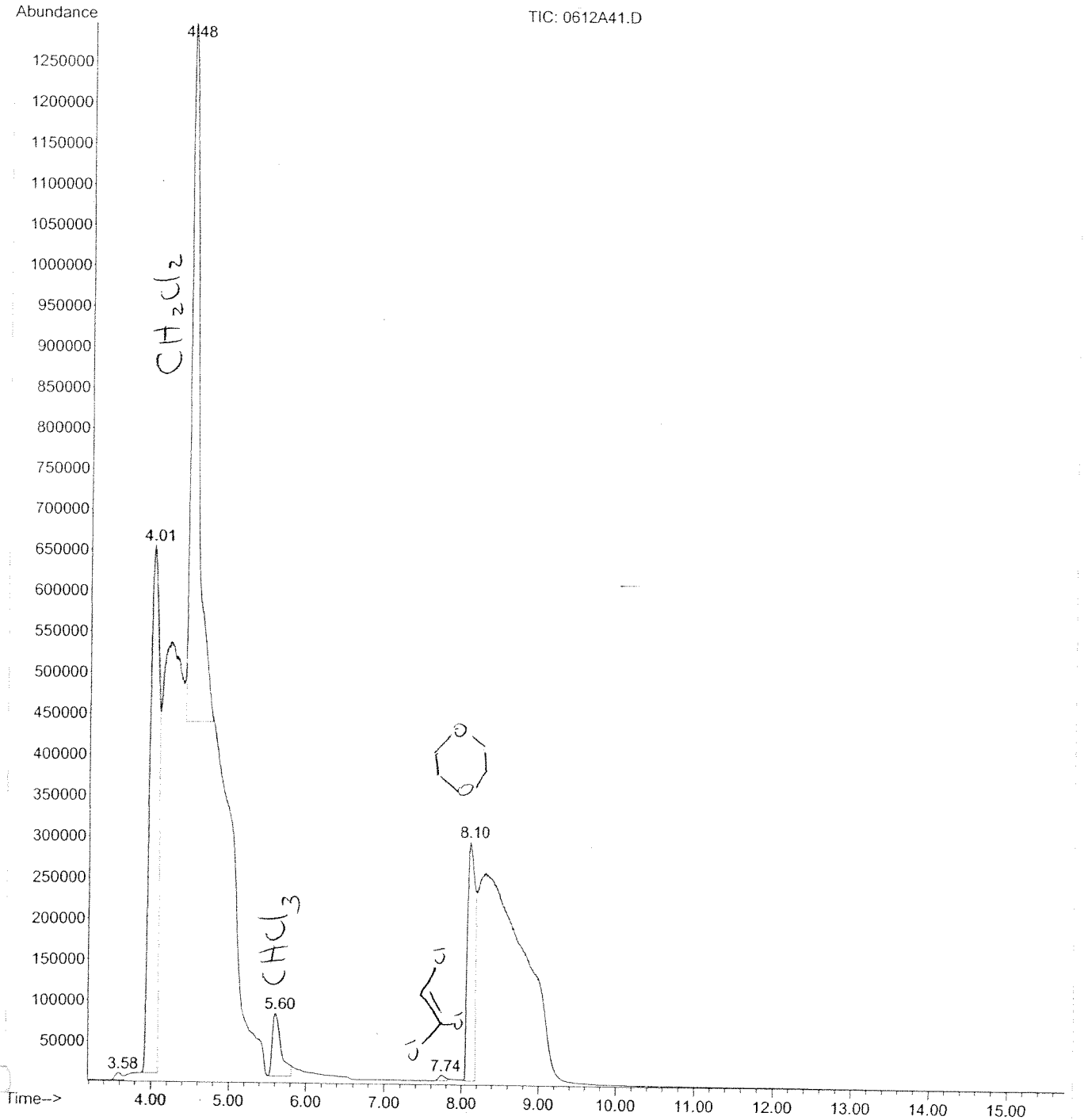


File : C:\MSDCHEM\1\DATA\OVI\0612A41.D
Operator : sly
Acquired : 14 Jun 2007 4:37 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS1
Misc Info :
Vial Number: 3

Sample # 377410
Attachment B pg 30 of 33
SLY 6-15-07



File : C:\MSDCHEM\1\DATA\OVI\0612A43.D
Operator : sly
Acquired : 14 Jun 2007 5:39 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 396200 desmopressin
Misc Info :
Vial Number: 20

Sample # 377410
Attachment 6 pg 31 of 33
SLY
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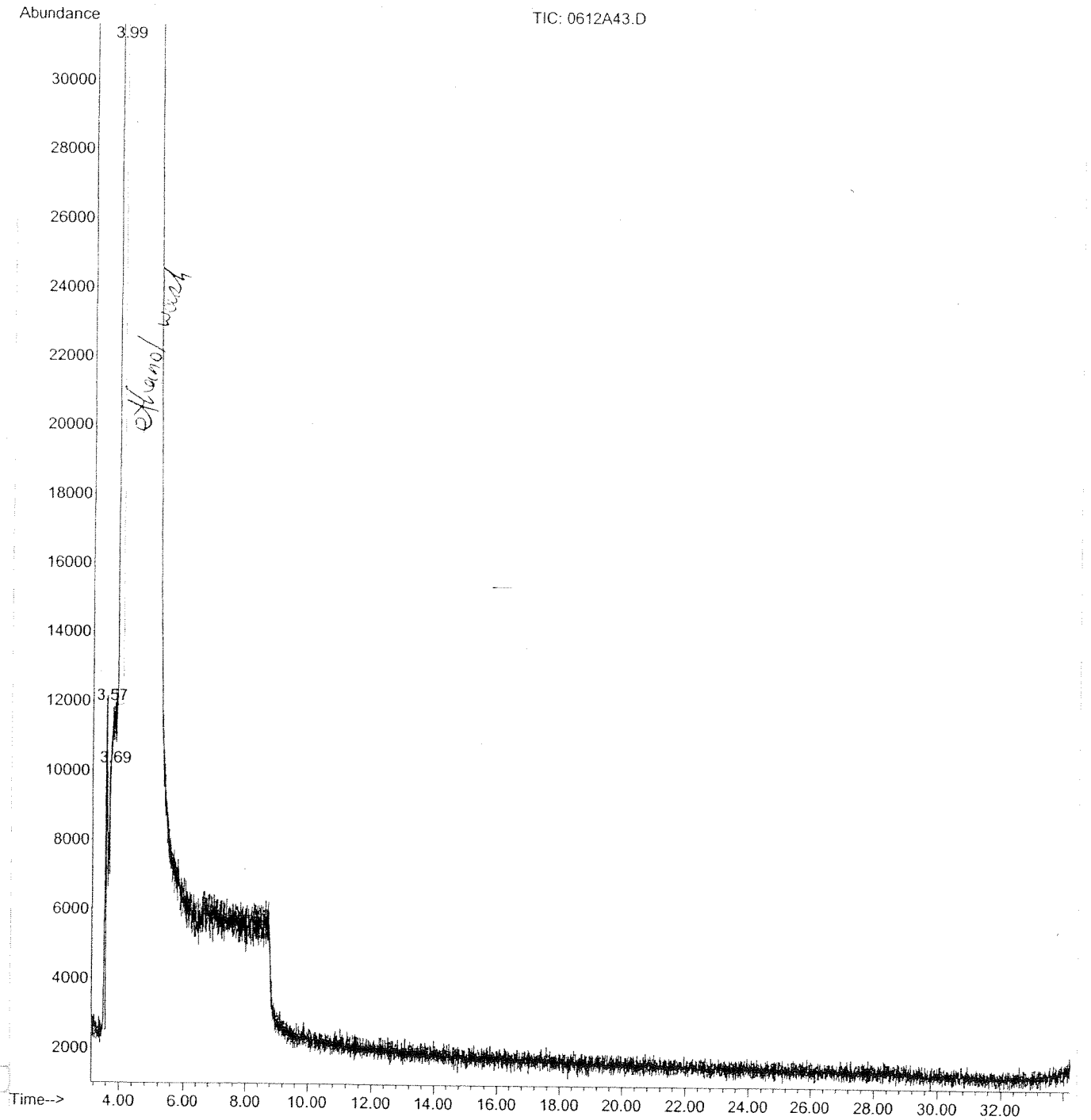

File : C:\MSDCHEM\1\DATA\OVI\0612A45.D
Operator : sly
Acquired : 14 Jun 2007 6:40 using AcqMethod OVI
Instrument : Instrumen
Sample Name: 420503 desmopressin
Misc Info :
Vial Number: 21

Sample # 377410
Attachment B pg 32 of 33
SLY
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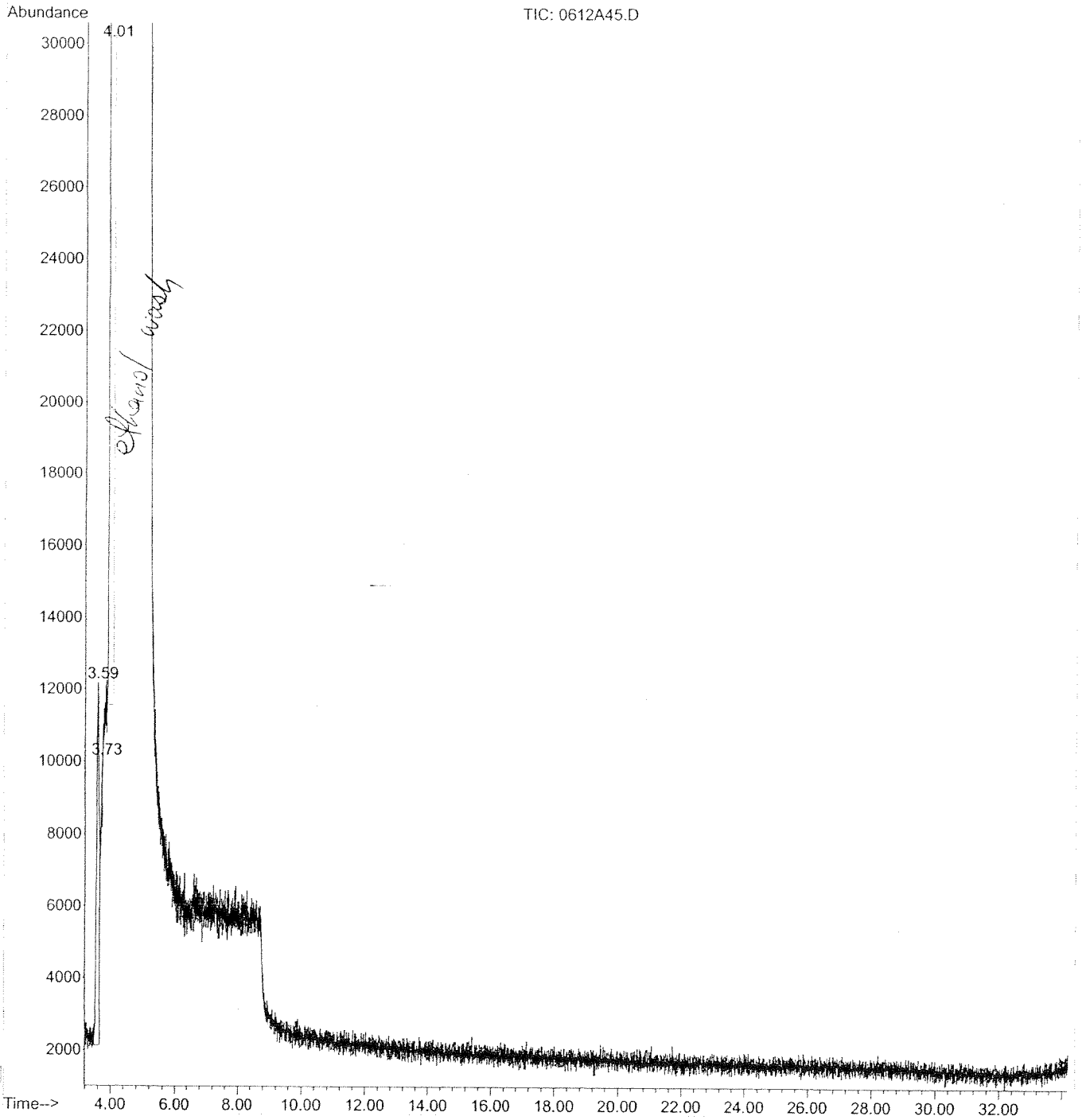
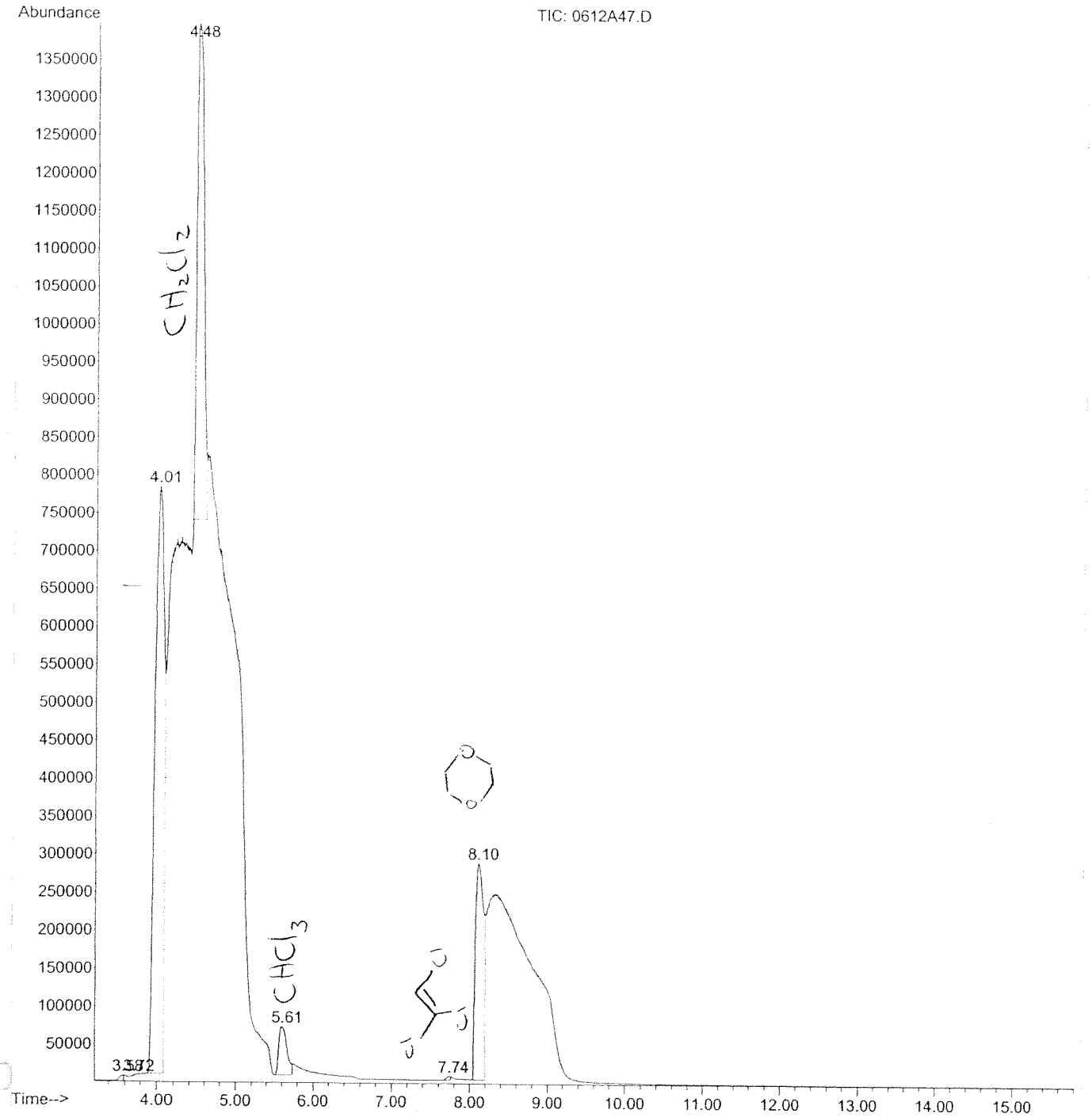


File : C:\MSDCHEM\1\DATA\OVI\0612A47.D
Operator : sly
Acquired : 14 Jun 2007 7:41 using AcqMethod OVI
Instrument : Instrumen
Sample Name: WS1
Misc Info :
Vial Number: 3

Sample # 377410
Attachment B pg 33 of 33
SLY 6-15-07



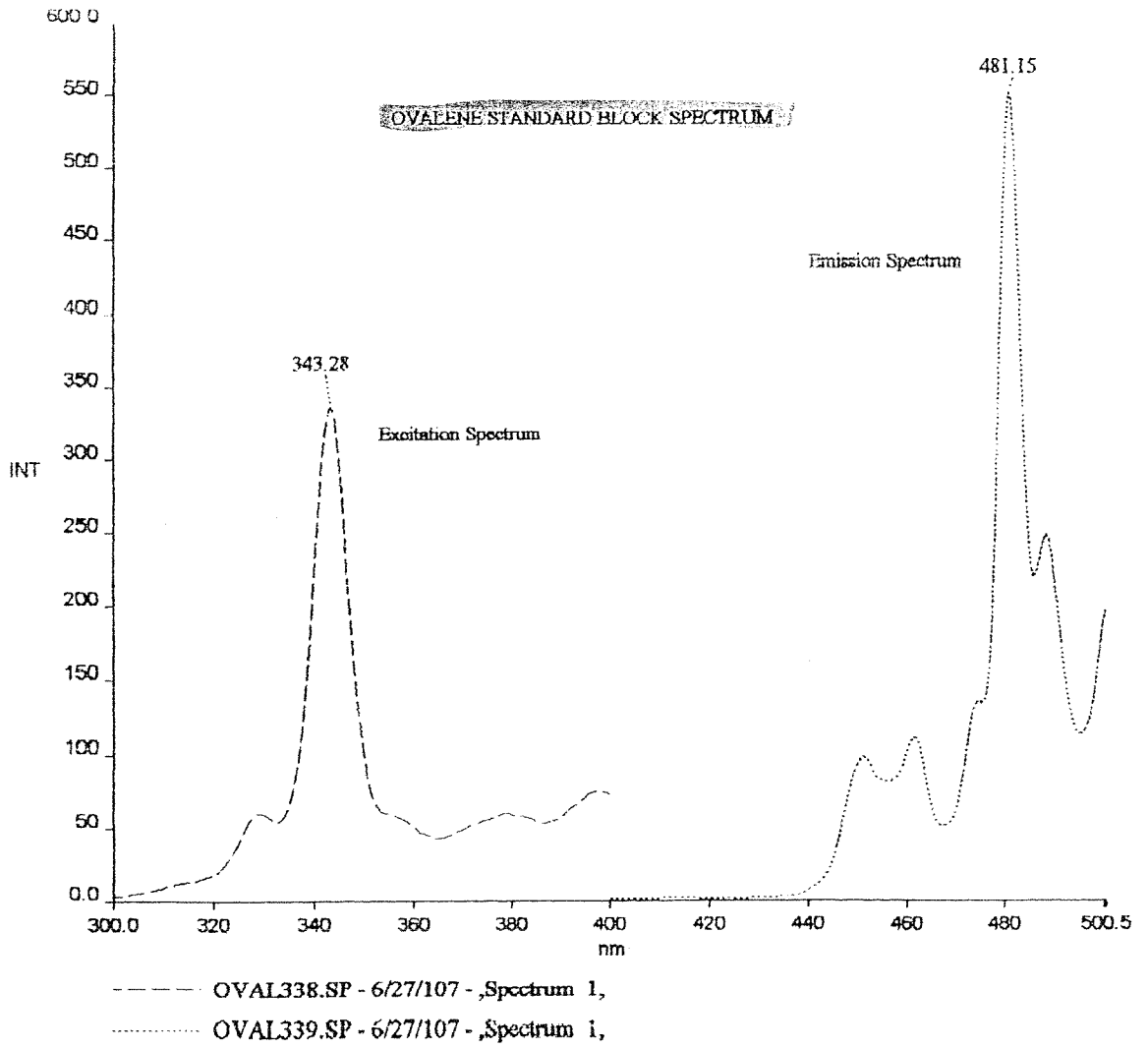
377410
6-29-07
SLY

Attachment C

Fluorescence Intensities
+ QC

Sample # 37740
Attachment C pg 1 of 3
SLY 6-29-07

Date: 6/27/107 Time: 12:52:20 PM



Sample # 377410
Attachment C pg 2 of 3
SLY 6-29-07

PerKin-Elmer LS50
Luminescence Spectrometer
Serial # 3057
FDA#1701410

Computer FDA#1700050

Software: FLWinLab
Version # 2.01
Copyright 1994-1997
PE Corp.

'l Concentration results
ienerated on :06-27-2007, at time:15:21:55
****
leasurement conditions
lethod:C:\FLWINLAB\METHODS\DIGOXIN.MTH
ser name: LLM
:omments: Default concentration method

:x. wavelength (nm):	372
:m. wavelength (nm):	465
:x. slit (nm):	10
:m. slit (nm):	10
ntegration time (s):	1
:m filter:	390 cut_off

****
:eference sample results

Std#	(Conc * Factor) (ng/mL)	Intensity
lank	0.000	0.945
a	50.000	7.123
-	100.000	8.788
	150.000	12.966
a	200.000	16.935
a	250.000	20.851
lank	0.000	0.881
b	50.000	5.199
b	100.000	9.253
b	150.000	12.934
b	200.000	16.418
b	250.000	21.165

i equation	Y=MX+C
lope	0.078
ntercept	1.411
orrelation	0.9958

****
nknown sample results
urrent samples filename: C:\FLWINLAB\DATA\DIGLLM.UNK

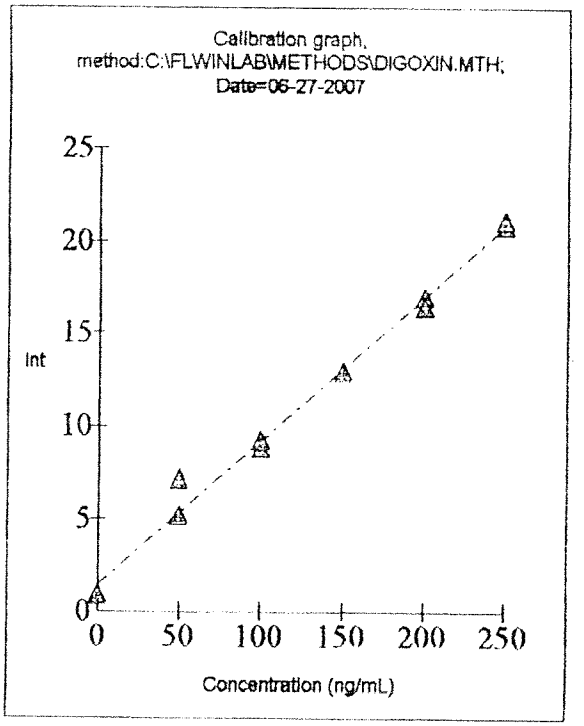
Sample	(Conc * Factor) (ng/mL)	Intensity
ab 1a	268.361	21.685
ab 2a	244.811	20.029
ab 3a	269.357	21.755
ab 4a	253.315	20.627
ab 5a	283.592	22.756
ab 6a	256.813	20.873
CV150a	142.402	12.828
ab 1b	261.092	21.694
ab 2b	245.208	20.460
3b	252.880	21.056
4b	243.715	20.344
5b	248.593	20.723
ab 6b	257.848	21.442
CV150b	146.220	12.770

Linear Regression concentration + samples results not used —

Program did not minus the blank or avg the sample intensities.

Sample results calculated with new line generated in Excel.

Sample # 377410
Attachment C pg 3 of 3
SLY 6-29-07



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Attachment D

QC spreadsheet for Assay/UDU

Attachment D p1 of 1

Printed on 7/2/2007 at 11:51 AM hrs

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Run #	041207SY	Date performed	12-Apr-07
Analyte/Parameter	digoxin	Matrix	tablet
Method(s)	USP digoxin tablets	Instrument	HPLC#1701616
Analyst			

Cal Lot #	USP O0B096		ICV Lot #			Matrices (ex)	Sample Number(s)
Cal Exp. Date			ICV Exp. Date			ss=semisol	
Cal1 Conc.	0.0411	mg/mL	ICV Conc	0.0427	mg/mL	s=solid	377410
			Sample Weight:	842.7	mg	l=liquid	
CCV Lot #			Sample Volume:		ml	oil	
CCV Exp. Date			QC Lot #				
CCV Conc.	0.0411	mg/mL	QC Exp. Date				
Spike Conc.	0.533	mg	QC Conc.	0.0514	mg/ml		
Spike Wt.			MDL	0.0206			

Avg Tablet Wt:	105.235	mg	Sample Wt. 2:	852.7	mg

Version #1.5

#	Sample ID	DF	Instrument Response	Initial Conc.	QC Result	Matrix	Sample Number	Result mg/mL	Result	Other	Other	Sig Figs
1												3
2	(ICal 1)		909.88556									3
3												
4												
5	a377410	25	856.10645	-	-		-	0.9668	0	966.8ug/8.0 tabs=120.8		4
6	z377410	25	860.05627	-	-		-	0.9712	0	971.2ug/8.1 tabs=120.0		4
7	ICV	1	951.14551	-	100.6%		-	0.042964	-			6
8	CCV	1	924.38165	-	101.7%		-	0.0418	-			4
9	CCV	1	916.10974	-	100.7%		-	0.0414	-			4
10	qhigh	1	1172.6206	-	103.1%		-	0.053	-			4
11	1MDL	1	468.1449	-	-		1MDL	0.0211	-			4
12	2MDL	1	462.41983	-	-		2MDL	0.0209	-			4
13	3MDL	1	461.31964	-	-		3MDL	0.0208	-			4
14	spike	25	903.54938	0.47	103.2%		-	1.0203	-			4
15	udu1	3	890.91492	-	-		-	0.1207	-	96.7		4
16	udu2	3	862.61694	-	-		-	0.1169	-	93.6		4
17	udu3	3	880.40179	-	-		-	0.1193	-	95.5		4
18	udu4	3	881.50073	-	-		-	0.1195	-	95.6		4
19	udu5	3	892.34027	-	-		-	0.1209	-	96.8		4
20	udu6	3	887.99988	-	-		-	0.1203	-	96.3		4
21	udu7	3	890.26398	-	-		-	0.1206	-	96.6		4
22	udu8	3	928.09546	-	-		-	0.1258	-	100.7		4
23	udu9	3	907.32068	-	-		-	0.123	-	98.4		4
24	udu10	3	897.28046	-	-		-	0.1216	-	97.3		4
25		1		-	-		-	#VALUE!	-			4

Calculations performed by Excel 2002/ Validated 3/18/03 CB

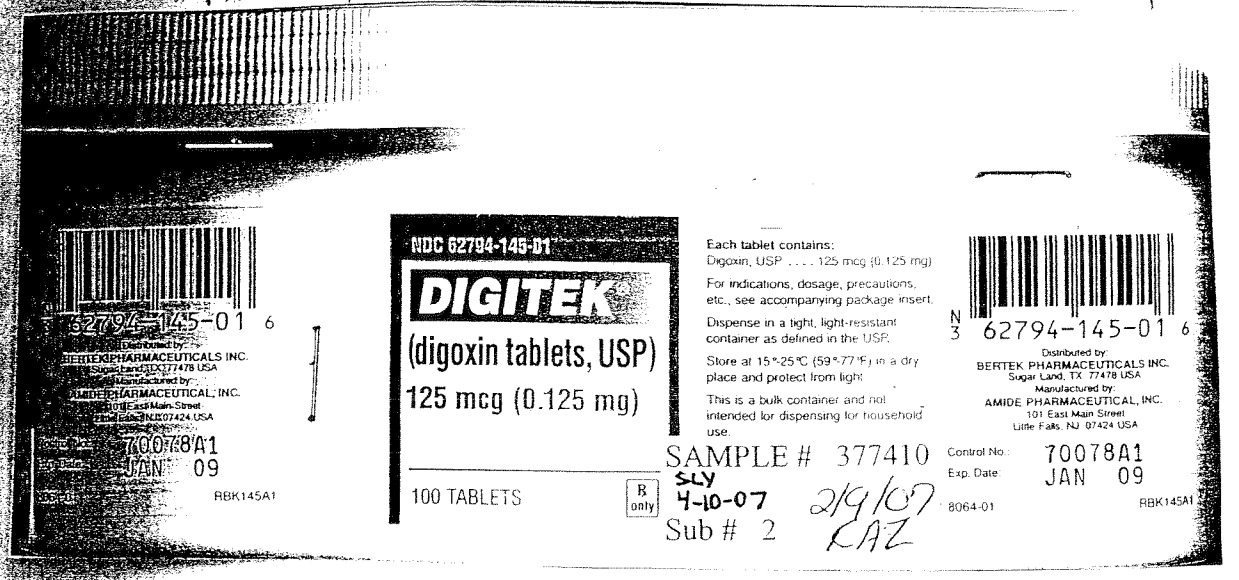
Entered by:

Reviewed by:

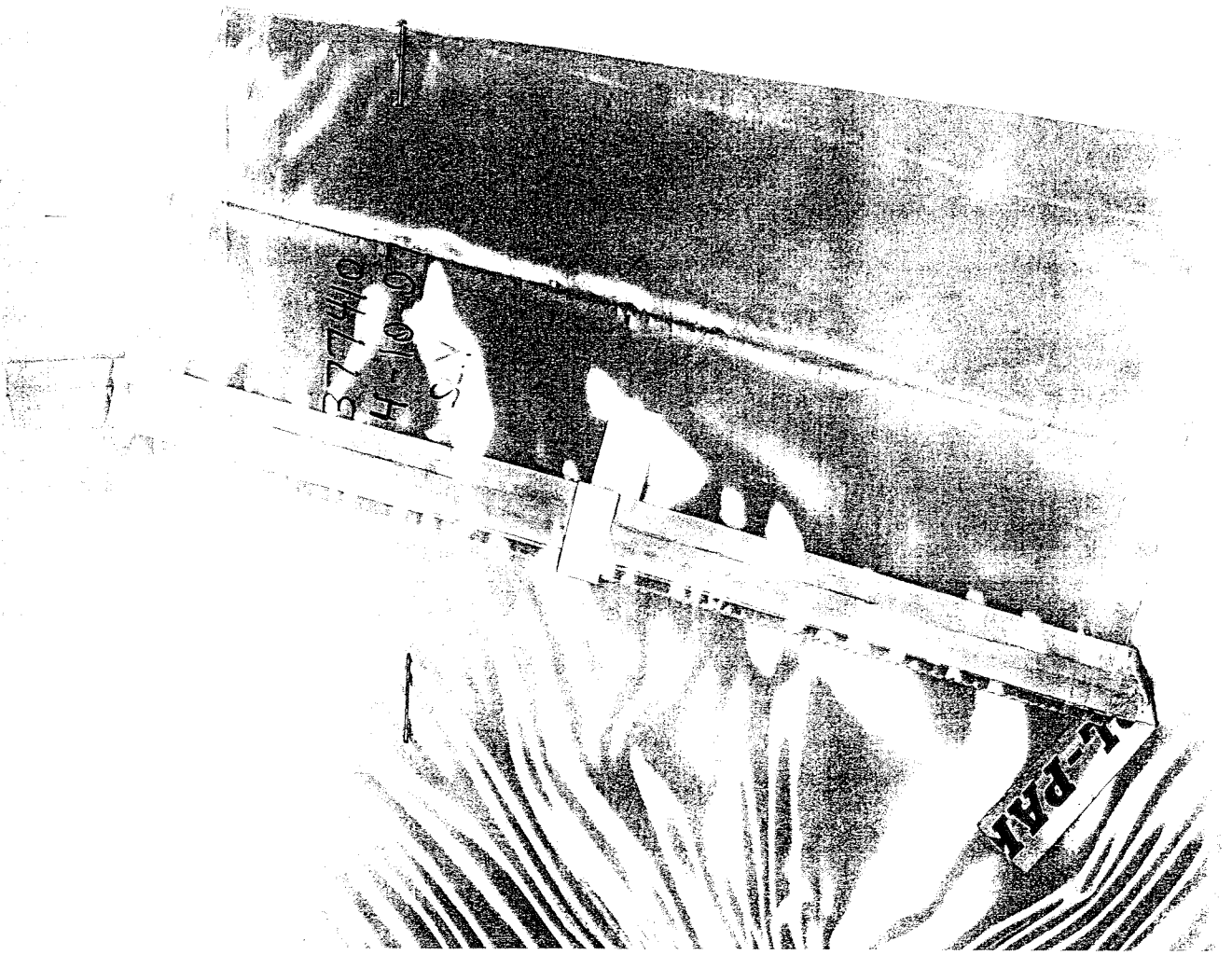
Labeling

377410
4-10-07
SLY

Photocopy of label on bottle



Original insert



reproduction studies have not been conducted with digoxin. It is also not known whether digoxin can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Digoxin should be given to a pregnant woman only if clearly needed.

Nursing Mothers: Studies have shown that digoxin concentrations in the mother's serum and milk are similar. However, the estimated exposure of a nursing infant to digoxin via breast feeding will be far below the usual infant maintenance dose. Therefore, this amount should have no pharmacologic effect upon the infant. Nevertheless, caution should be exercised when digoxin is administered to a nursing woman.

Pediatric Use: Newborn infants display considerable variability in their tolerance to digoxin. Premature and immature infants are particularly sensitive to the effects of digoxin, and the dosage of the drug must not only be reduced but must be individualized according to their degree of maturity. Digitalis glycosides can cause poisoning in children due to accidental ingestion.

Geriatric Use: The majority of clinical experience gained with digoxin has been in the elderly population. This experience has not identified differences in response or adverse effects between the elderly and younger patients. However, this drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, which should be based on renal function, and it may be useful to monitor renal function (see DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS: In general, the adverse reactions of digoxin are dose-dependent and occur at doses higher than those needed to achieve a therapeutic effect. Hence, adverse reactions are less common when digoxin is used within the recommended dose range or therapeutic serum concentration range and when there is careful attention to concurrent medications and conditions.

Because some patients may be particularly susceptible to side effects with digoxin, the dosage of the drug should always be selected carefully and adjusted as the clinical condition of the patient warrants. In the past, when high doses of digoxin were used and little attention was paid to clinical status or concurrent medications, adverse reactions to digoxin were more frequent and severe. Cardiac adverse reactions accounted for about one-half, gastrointestinal disturbances for about one-fourth, and CNS and other toxicity for about one-fourth of these adverse reactions. However, available evidence suggests that the incidence and severity of digoxin toxicity has decreased substantially in recent years. In recent controlled clinical trials, in patients with predominantly mild to moderate heart failure, the incidence of adverse experiences was comparable in patients taking digoxin and in those taking placebo. In a large mortality trial, the incidence of hospitalization for suspected digoxin toxicity was 2% in patients taking digoxin compared to 0.9% in patients taking placebo. In this trial, the most common manifestations of digoxin toxicity included gastrointestinal and cardiac disturbances; CNS manifestations were less common.

Adults: ***Cardiac:*** Therapeutic doses of digoxin may cause heart block in patients with pre-existing sinoatrial or AV conduction disorders; heart block can be avoided by adjusting the dose of digoxin. Prophylactic use of a cardiac pacemaker may be considered if the risk of heart block is considered unacceptable. High doses of digoxin may produce a variety of rhythm disturbances, such as first-degree, second-degree (Wenckebach), or third-degree heart block (including asystole); atrial tachycardia with block; AV dissociation; accelerated junctional (nodal) rhythm; unifocal or multiform ventricular premature contractions (especially bigeminy or trigeminy), ventricular tachycardia; and ventricular fibrillation. Digoxin produces PR prolongation and ST segment depression which should not by themselves be considered digoxin toxicity. Cardiac toxicity can also occur at therapeutic doses in patients who have conditions which may alter their sensitivity to digoxin (see WARNINGS and PRECAUTIONS).

Gastrointestinal: Digoxin may cause anorexia, nausea, vomiting and diarrhea. Rarely, the use of digoxin has been associated with abdominal pain, intestinal ischemia, and hemorrhagic necrosis of the intestines.

CNS: Digoxin can produce visual disturbances (blurred or yellow vision), headache, weakness, dizziness, apathy, confusion and mental disturbances (such as anxiety, depression, delirium, and hallucination).

Other: Gynecomastia has been occasionally observed following the prolonged use of digoxin. Thrombocytopenia and maculopapular rash and other skin reactions have been rarely observed.

The following table summarizes the incidence of those adverse experiences listed above for patients treated with digoxin tablets or placebo from two randomized, double-blind, placebo-controlled withdrawal trials. Patients in these trials were also receiving diuretics with or without angiotensin-converting enzyme inhibitors. These patients have been stable on digoxin, and were randomized to digoxin or placebo. The results shown in Table 4 reflect the experience in patients following dosage titration with the us[illegible]um digoxin concentrations and careful follow-up. These ad[illegible]iences are consistent with results from a large, pla[illegible]rtality trial (DIG trial) wherein over half the patie[illegible]ol receiving digoxin prior to enrollment.

Table 4: Adverse Experiences in Two Parallel, Double-Blind, Placebo-Controlled Withdrawal Trials (Number of Patients Reporting)

Adverse Experience	Digoxin Patients (n=123)	Placebo Patients (n=125)
Cardiac		
Palpitation	1	4
Ventricular extrasystole	1	1
Tachycardia	2	1
Heart arrest	1	1
Gastrointestinal		
Anorexia	1	4
Nausea	4	2
Vomiting	2	1
Diarrhea	4	1
Abdominal pain	0	6
CNS		
Headache	4	4
Dizziness	6	5
Mental disturbances	5	1
Other		
Rash	2	1
Death	4	3

Infants and Children: The side effects of digoxin in infants and children differ from those seen in adults in several respects. Although digoxin may produce anorexia, nausea, vomiting, diarrhea, and CNS disturbances in young patients, these are rarely the initial symptoms of overdosage. Rather, the earliest and most frequent manifestation of excessive dosing with digoxin in infants and children is the appearance of cardiac arrhythmias, including sinus bradycardia. In children, the use of digoxin may produce any arrhythmia. The most common are conduction disturbances or supraventricular tachyarrhythmias, such as atrial tachycardia (with or without block) and junctional (nodal) tachycardia. Ventricular arrhythmias are less common. Sinus bradycardia may be a sign of impending digoxin intoxication, especially in infants, even in the absence of first-degree heart block. Any arrhythmia or alteration in cardiac conduction that develops in a child taking digoxin should be assumed to be caused by digoxin, until further evaluation proves otherwise.

OVERDOSAGE:

Treatment of Adverse Reactions Produced by Overdosage: Digoxin should be temporarily discontinued until the adverse reaction resolves. Every effort should also be made to correct factors that may contribute to the adverse reaction (such as electrolyte disturbances or concurrent medications). Once the adverse reaction has resolved, therapy with digoxin may be reinstituted, following a careful reassessment of dose.

Withdrawal of digoxin may be all that is required to treat the adverse reaction. However, when the primary manifestation of digoxin overdosage is a cardiac arrhythmia, additional therapy may be needed.

If the rhythm disturbance is a symptomatic bradyarrhythmia or heart block, consideration should be given to the reversal of toxicity with DIGIBIND® [Digoxin Immune Fab (Ovine)] (see below), the use of atropine, or the insertion of a temporary cardiac pacemaker. However, asymptomatic bradycardia or heart block related to digoxin may require only temporary withdrawal of the drug and cardiac monitoring of the patient.

If the rhythm disturbance is a ventricular arrhythmia, consideration should be given to the correction of electrolyte disorders, particularly if hypokalemia (see below) or hypomagnesemia is present. DIGIBIND® [Digoxin Immune Fab (Ovine)] is a specific antidote for digoxin and may be used to reverse potentially life-threatening ventricular arrhythmias due to digoxin overdosage.

Administration of Potassium: Every effort should be made to maintain the serum potassium concentration between 4 and 5.5 mmol/L. Potassium is usually administered orally, but when correction of the arrhythmia is urgent and the serum potassium concentration is low, potassium may be administered cautiously by the intravenous route. The electrocardiogram should be monitored for any evidence of potassium toxicity (e.g., peaking of T waves) and to observe the effect on the arrhythmia. Potassium salts may be dangerous in patients who manifest bradycardia or heart block due to digoxin (unless primarily related to supraventricular tachycardia) and in the setting of massive digitalis overdosage (see Massive Digitalis Overdosage subsection).

Massive Digitalis Overdosage: Manifestations of life-threatening toxicity include ventricular tachycardia or ventricular fibrillation, or progressive bradyarrhythmias, or heart block. The administration of more than 10 mg of digoxin in a previously healthy adult or more than 4 mg in a previously healthy child, or a steady-state serum concentration greater than 10 ng/mL often results in cardiac arrest.

DIGIBIND® [Digoxin Immune Fab (Ovine)] should be used to reverse the toxic effects of ingestion of a massive overdose. The decision to administer DIGIBIND® [Digoxin Immune Fab (Ovine)] to a patient who has ingested a massive dose of digoxin but who has not yet manifested life-threatening toxicity should depend on the likelihood that life-threatening toxicity will occur (see above).

Patients with massive digitalis ingestion should receive large doses of activated charcoal to prevent absorption and bind digoxin in the gut during enterocenteric recirculation. Emesis or gastric lavage may be indicated especially if ingestion has occurred within 30 minutes of the patient's presentation at the hospital. Emesis should not be induced in patients who are obtunded. If a patient presents more than 2 hours after ingestion or already has toxic manifestations, it may be unsafe to induce vomiting or attempt passage of a gastric tube, because such maneuvers may induce an acute vagal episode that can worsen digitalis-related arrhythmias.

Severe digitalis intoxication can cause a massive shift of potassium from inside to outside the cell, leading to life-threatening hyperkalemia. The administration of potassium supplements in the setting of massive intoxication may be hazardous and should be avoided. Hyperkalemia caused by massive digitalis toxicity is best treated with DIGIBIND® [Digoxin Immune Fab (Ovine)]; initial treatment with glucose and insulin may also be required if hyperkalemia itself is acutely life-threatening.

DOSAGE AND ADMINISTRATION:

General: Recommended dosages of digoxin may require considerable modification because of individual sensitivity of the patient to the drug, the presence of associated conditions, or the use of concurrent medications. In selecting a dose of digoxin, the following factors must be considered:

1. The body weight of the patient. Doses should be calculated based upon lean (i.e., ideal) body weight.
2. The patient's renal function, preferably evaluated on the basis of estimated creatinine clearance.
3. The patient's age. Infants and children require different doses of digoxin than adults. Also, advanced age may be indicative of diminished renal function even in patients with normal serum creatinine concentration (i.e., below 1.5 mg/dL).
4. Concomitant disease states, concurrent medications, or other factors likely to alter the pharmacokinetic or pharmacodynamic profile of digoxin (see PRECAUTIONS).

Serum Digoxin Concentrations: In general, the dose of digoxin used should be determined on clinical grounds. However, measurement of serum digoxin concentrations can be helpful to the clinician in determining the adequacy of digoxin therapy and in assigning certain probabilities to the likelihood of digoxin intoxication. About two-thirds of adults considered adequately digitalized (without evidence of toxicity) have serum digoxin concentrations ranging from 0.8 to 2 ng/mL. However, digoxin may produce clinical benefits even at serum concentrations below this range. About two-thirds of adult patients with clinical toxicity have serum digoxin concentrations greater than 2 ng/mL. However, since one third of patients with clinical toxicity have concentrations less than 2 ng/mL, values below 2 ng/mL do not rule out the possibility that a certain sign or symptom is related to digoxin therapy. Rarely, there are patients who are unable to tolerate digoxin at serum concentrations below 0.8 ng/mL. Consequently, the serum concentration of digoxin should always be interpreted in the overall clinical context, and an isolated measurement should not be used alone as the basis for increasing or decreasing the dose of the drug.

To allow adequate time for equilibration of digoxin between serum and tissue, sampling of serum concentrations should be done just before the next scheduled dose of the drug. If this is not possible, sampling should be done at least 6 to 8 hours after the last dose, regardless of the route of administration or the formulation used. On a once-daily dosing schedule, the concentration of digoxin will be 10% to 25% lower when sampled at 24 verses 8 hours, depending upon the patient's renal function. On a twice-daily dosing schedule, there will be only minor differences in serum digoxin concentrations whether sampling is done at 8 or 12 hour after a dose.

If a discrepancy exists between the reported serum concentration and the observed clinical response, the clinician should consider the following possibilities:

1. Analytical problems in the assay procedure.
2. Inappropriate serum sampling time.
3. Administration of a digitalis glycoside other than digoxin.
4. Conditions (described in WARNINGS and PRECAUTIONS) causing an alteration in the sensitivity of the patient to digoxin.
5. Serum digoxin concentration may decrease acutely during periods of exercise without any associate change in clinical efficacy due to increased binding of digoxin to skeletal muscle.

Heart Failure: ***Adults:*** Digitalization may be accomplished by either of two general approaches that vary in dosage and frequency of administration, but reach the same endpoint in terms of total amount of digoxin accumulated in the body.

1. If rapid digitalization is considered medically appropriate, it may be achieved by administering a loading dose based upon projected peak digoxin body stores. Maintenance dose can be calculated as a percentage of the load[illegible]ose.
2. More gradual digitalization may be [illegible]y beginning an appropriate maintenance dose, t[illegible]g digoxin body stores to accumulate slowly. Steady [illegible]um digoxin concentrations will be achieved in approximately five half-lives of the drug for the individual patient. Depending upon the patient's renal function, this will take between 1 and 3 weeks.

Rapid Digitalization with a Loading Dose: Peak digoxin body stores of 8 to 12 mcg/kg should provide therapeutic effect with minimum risk of toxicity in most patients with heart failure and normal sinus rhythm. Because of altered digoxin distribution and elimination, projected peak body stores for patients with renal insufficiency should be conservative (i.e., 6 to 10 mcg/kg) (see PRECAUTIONS).

The loading dose should be administered in several portions, with roughly half the total given as the first dose. Additional fractions of this planned total dose may be given at 6- to 8-hour intervals, **with careful assessment of clinical response before each additional dose.**

If the patient's clinical response necessitates a change from the calculated loading dose of digoxin, then calculation of the maintenance dose should be based upon the amount actually given.

A single initial dose of 500 to 750 mcg (0.5 to 0.75 mg) of digoxin tablets usually produces a detectable effect in 0.5 to 2 hours that becomes maximal in 2 to 6 hours. Additional doses of 125 to 375 mcg (0.125 to 0.375 mg) may be given cautiously at 6- to 8-hour intervals until clinical evidence of an adequate effect is noted. The usual amount of digoxin tablets that a 70-kg patient requires to achieve 8 to 12 mcg/kg peak body stores is 750 to 1,250 mcg (0.75 to 1.25 mg).

Digoxin Injection is frequently used to achieve rapid digitalization, with conversion to digoxin tablets or Digoxin Solution in Capsules for maintenance therapy. If patients are switched from intravenous to oral digoxin formulations, allowances must be made for differences in bioavailability when calculating maintenance dosages (see table, CLINICAL PHARMACOLOGY).

Maintenance Dosing: The doses of digoxin used in controlled trials in patients with heart failure have ranged from 125 to 500 mcg (0.125 to 0.5 mg) once daily. In these studies, the digoxin dose has been generally titrated according to the patient's age, lean body weight, and renal function. Therapy is generally initiated at a dose of 250 mcg (0.25 mg) once daily in patients under age 70 with good renal function, at a dose of 125 mcg (0.125 mg) once daily in patients over age 70 or with impaired renal function, and at a dose of 62.5 mcg (0.0625 mg) in patients with marked renal impairment. Doses may be increased every 2 weeks according to clinical response.

In a subset of approximately 1,800 patients enrolled in the DIG trial (wherein dosing was based on an algorithm similar to that in Table 5) the mean (±SD) serum digoxin concentrations at 1 month and 12 months were 1.01 ± 0.47 ng/mL and 0.97 ± 0.43 ng/mL, respectively.

The maintenance dose should be based upon the percentage of the peak body stores lost each day through elimination. The following formula has had wide clinical use:

Maintenance Dose = Peak Body Stores (i.e., Loading Dose) x % Daily Loss/100

Where: % Daily Loss = 14 + Ccr/5

(Ccr is creatinine clearance, corrected to 70 kg body weight or 1.73 m^2 body surface area.)

Table 5 provides average daily maintenance dose requirements of digoxin tablets for patients with heart failure based upon lean body weight and renal function:

Table 5: Usual Daily Maintenance Dose Requirements (mcg) of Digoxin for Estimated Peak Body Stores of 10 mcg/kg

Corrected Ccr (mL/min per 70 kg)*	Lean Body Weight kg	50	60	70	80	90	100	Number of Days Before Steady-State Achieved†
	lb	110	132	154	176	198	220	
0		62.5‡	125	125	125	187.5	187.5	22
10		125	125	125	187.5	187.5	187.5	19
20		125	125	187.5	187.5	187.5	250	16
30		125	187.5	187.5	187.5	250	250	14
40		125	187.5	187.5	250	250	250	13
50		187.5	187.5	250	250	250	250	12
60		187.5	187.5	250	250	250	375	11
70		187.5	250	250	250	250	375	10
80		187.5	250	250	250	375	375	9
90		187.5	250	250	250	375	500	8
100		250	250	250	375	375	500	7

*Ccr is creatinine clearance, corrected to 70 kg body weight or 1.73 m^2 body surface area. *For adults*, if only serum creatinine concentrations (Scr) are available, a Ccr (corrected to 70 kg body weight) may be estimated in men as (140-Age)/Scr. For women, this result should be multiplied by 0.85.

Note: This equation cannot be used for estimating creatinine clearance in infants or children.

†If no loading dose administered

‡62.5 mcg = 0.0625 mg

Example: Based on the above table, a patient in heart failure with an estimated lean body weight of 70 kg and a Ccr of 60 mL/min, should be given a dose of 250 mcg (0.25 mg) daily of digoxin tablets, usually taken after the morning meal. If no loading dose is administered, steady-state serum concentrations in this patient should be anticipated at approximately 11 days.

Infants and Children: In general, divided daily dosing is recommended for infants and young children (under age 10). In the newborn period, renal clearance of digoxin is diminished and suitable dosage adjustments must be observed. This is especially pronounced in the premature infant. Beyond the immediate newborn period, children generally require proportionally larger doses than adults on the basis of body weight or body surface area. Children over 10 years of age require adult dosages in proportion to their body weight. Some researchers have suggested that infants and young children tolerate slightly higher serum concentrations than do adults.

Daily maintenance doses for each age group are given in Table 6 and should provide therapeutic effects with minimum risk of toxicity in most patients with heart failure and normal sinus rhythm. These recommendations assume the presence of normal renal function:

Table 6: Daily Maintenance Doses in Children with Normal Renal Function

Age	Daily Maintenance Dose (mcg/kg)
2 to 5 years	10 to 15
5 to 10 years	7 to 10
Over 10 years	3 to 5

In children with renal disease, digoxin must be carefully titrated based upon clinical response.

It cannot be overemphasized that both the adult and pediatric dosage guidelines provided are based upon average patient response and substantial individual variation can be expected. Accordingly, ultimate dosage selection must be based upon clinical assessment of the patient.

Atrial Fibrillation: Peak digoxin body stores larger than the 8 to 12 mcg/kg required for most patients with heart failure and normal sinus rhythm have been used for control of ventricular rate in patients with atrial fibrillation. Doses of digoxin used for the treatment of chronic atrial fibrillation should be titrated to the minimum dose that achieves the desired ventricular rate control without causing undesirable side effects. Data are not available to establish the appropriate resting or exercise target rates that should be achieved.

Dosage Adjustment When Changing Preparations: The difference in bioavailability between Digoxin Injection or Digoxin Solution in Capsules and Digoxin Pediatric Elixir or digoxin tablets must be considered when changing patients from one dosage form to another.

Doses of 100 mcg (0.1 mg) and 200 mcg (0.2 mg) of Digoxin Solution in Capsules are approximately equivalent to 125-mcg (0.125-mg) and 250-mcg (0.25-mg) doses of digoxin tablets and Pediatric Elixir, respectively. (see table in CLINICAL PHARMACOLOGY: Pharmacokinetics).

HOW SUPPLIED:

DIGITEK® (digoxin tablets, USP) 125 mcg (0.125 mg) are yellow, round tablets, and imprinted with **B 145** on the scored side of the tablet. They are available as follows:

NDC 62794-145-01
bottles of 100 tablets
NDC 62794-145-10
bottles of 1000 tablets
NDC 62794-145-56
bottles of 5000 tablets

DIGITEK™ (digoxin tablets, USP) 250 mcg (0.25 mg) are white, round tablets, and imprinted with **B 146** on the scored side of the tablet. They are available as follows:

NDC 62794-146-01
bottles of 100 tablets
NDC 62794-146-10
bottles of 1000 tablets
NDC 62794-146-56
bottles of 5000 tablets

Store at 15° to 25°C (59° to 77°F) in a dry place and protect from light.

Dispense in a tight, light-resistant container as defined in the USP.

REVISED NOVEMBER 2000
BKDGTK.R4

8070-02

Distributed by:
BERTEK PHARMACEUTICALS INC.
Sugar Land, TX 77478 USA

Manufactured by:
AMIDE PHARMACEUTICAL, I[illegible]
101 East Main Street, Little Falls, NJ 0[illegible] USA

DIGITEK®
(digoxin tablets, USP)

℞ only

DESCRIPTION: DIGITEK (digoxin) is one of the cardiac (or digitalis) glycosides, a closely related group of drugs having in common specific effects on the myocardium. These drugs are found in a number of plants. Digoxin is extracted from the leaves of *Digitalis lanata*. The term "digitalis" is used to designate the whole group of glycosides. The glycosides are composed of two portions: a sugar and a cardenolide (hence "glycosides").

Digoxin is described chemically as (3 β, 5 β, 12 β)-3-[(2, 6-dideoxy-β-*D-ribo*-hexopyranosyl-(1→4)-(2,6-dideoxy-β-*D-ribo*-hexopyranosyl-(1→4)-2,6-dideoxy-β-*D-ribo*-hexopyranosyl)oxy]-12,14-dihydroxy-card-20(22)-enolide. Its molecular formula is $C_{41}H_{64}O_{14}$, its molecular weight is 780.94, and the structural formula shown.

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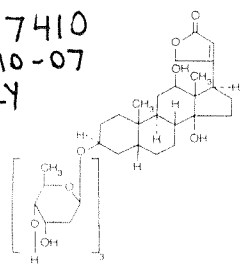

Digoxin exists as odorless white crystals that melt with decomposition above 230°C. The drug is practically insoluble in water and in ether; slightly soluble in diluted (50%) alcohol and in chloroform; and freely soluble in pyridine.

DIGITEK is supplied as 125-mcg (0.125-mg) or 250-mcg (0.25-mg) tablets for oral administration. Each tablet contains the labeled amount of digoxin USP and the following inactive ingredients: corn starch, croscarmellose sodium, microcrystalline cellulose, pregelatinized starch, lactose monohydrate and anhydrous lactose, silicon dioxide and stearic acid. In addition, the 125-mcg (0.125-mg) tablet contains D&C Yellow No. 10 Aluminum Lake.

CLINICAL PHARMACOLOGY: Mechanism of Action: Digoxin inhibits sodium-potassium ATPase, an enzyme that regulates the quantity of sodium and potassium inside cells. Inhibition of the enzyme leads to an increase in the intracellular concentration of sodium and thus (by stimulation of sodium-calcium exchange) an increase in the intracellular concentration of calcium. The beneficial effects of digoxin result from direct actions on cardiac muscle, as well as indirect actions on the cardiovascular system mediated by effects on the autonomic nervous system. The autonomic effects include: (1) a vagomimetic action, which is responsible for the effects of digoxin on the sinoatrial and atrioventricular (AV) nodes; and (2) baroreceptor sensitization, which results in increased afferent inhibitory activity and reduced activity of the sympathetic nervous system and renin-angiotensin system for any given increment in mean arterial pressure. The pharmacologic consequences of these direct and indirect effects are: (1) an increase in the force and velocity of myocardial systolic contraction (positive inotropic action); (2) a decrease in the degree of activation of the sympathetic nervous system and renin-angiotensin system (neurohormonal deactivating effect); and (3) slowing of the heart rate and decreased conduction velocity through the AV node (vagomimetic effect). The effects of digoxin in heart failure are mediated by its positive inotropic and neurohormonal deactivating effects, whereas the effects of the drug in atrial arrhythmias are related to its vagomimetic actions. In high doses digoxin increases sympathetic outflow from the central nervous system (CNS). This increase in sympathetic activity may be an important factor in digitalis toxicity.

Pharmacokinetics: ***Absorption:*** Follow[illegible] administration, peak serum concentrations of digoxin occur[illegible] hours. Absorption of digoxin from digoxin tablets has b[illegible]ed to be 60% to 80% complete compared to an id[illegible]venous dose of digoxin (absolute bioavailability) or Digoxin Solution in Capsules (relative bioavailability). When digoxin tablets are taken after meals, the rate of absorption is slowed, but the total amount of digoxin absorbed is usually unchanged. When taken with meals high in bran fiber, however, the amount absorbed from an oral dose may be reduced. Comparisons of the systemic availability and equivalent doses for oral preparations of digoxin are shown in Table 1:

Table 1: Comparisons of the Systemic Availability and Equivalent Doses for Oral Preparations of Digoxin

Product	Absolute Bio-availability	Equivalent Doses(mcg)* Among Dosage Forms			
Digoxin Tablets	60-80%	62.5	125	250	500
Digoxin Pediatric Elixir	70-85%	62.5	125	250	500
Digoxin Solution in Capsules	90-100%	50	100	200	400
Digoxin Injection/IV	100%	50	100	200	400

*For example, 125-mcg Digoxin Tablets equivalent to 125 mcg Digoxin Pediatric Elixir equivalent to 100 mcg Digoxin Solution in Capsules equivalent to 100 mcg Digoxin Injection/IV.

In some patients, orally administered digoxin is converted to inactive reduction products (e.g., dihydrodigoxin) by colonic bacteria in the gut. Data suggest that one in ten patients treated with digoxin tablets will degrade 40% or more of the ingested dose. As a result, certain antibiotics may increase the absorption of digoxin in such patients. Although inactivation of these bacteria by antibiotics is rapid, the serum digoxin concentration will rise at a rate consistent with the elimination half-life of digoxin. The magnitude of rise in serum digoxin concentration relates to the extent of bacterial inactivation, and may be as much as two-fold in some cases.

Distribution: Following drug administration, a 6-to 8-hour tissue distribution phase is observed. This is followed by a much more gradual decline in the serum concentration of the drug, which is dependent on the elimination of digoxin from the body. The peak height and slope of the early portion (absorption/distribution phases) of the serum concentration-time curve are dependent upon the route of administration and the absorption characteristics of the formulation. Clinical evidence indicates that the early high serum concentrations do not reflect the concentration of digoxin at its site of action, but that with chronic use, the steady-state post-distribution serum concentrations are in equilibrium with tissue concentrations and correlate with pharmacologic effects. In individual patients, these post-distribution serum concentrations may be useful in evaluating therapeutic and toxic effects (see DOSAGE AND ADMINISTRATION: Serum Digoxin Concentrations).

Digoxin is concentrated in tissues and therefore has a large apparent volume of distribution. Digoxin crosses both the blood-brain barrier and the placenta. At delivery, the serum digoxin concentration in the newborn is similar to the serum concentration in the mother. Approximately 25% of digoxin in the plasma is bound to protein. Serum digoxin concentrations are not significantly altered by large changes in fat tissue weight, so that its distribution space correlates best with lean (i.e., ideal) body weight, not total body weight.

Metabolism: Only a small percentage (16%) of a dose of digoxin is metabolized. The end metabolites, which include 3 β-digoxigenin, 3-keto-digoxigenin, and their glucuronide and sulfate conjugates, are polar in nature and are postulated to be formed via hydrolysis, oxidation, and conjugation. The metabolism of digoxin is not dependent upon the cytochrome P-450 system, and digoxin is not known to induce or inhibit the cytochrome P-450 system.

Excretion: Elimination of digoxin follows first-order kinetics (that is, the quantity of digoxin eliminated at any time is proportional to the total body content). Following intravenous administration to healthy volunteers, 50% to 70% of a digoxin dose is excreted unchanged in the urine. Renal excretion of digoxin is proportional to glomerular filtration rate and is largely independent of urine flow. In healthy volunteers with normal renal function, digoxin has a half-life of 1.5 to 2 days. The half-life in anuric patients is prolonged to 3.5 to 5 days. Digoxin is not effectively removed from the body by dialysis, exchange transfusion, or during cardiopulmonary bypass because most of the drug is bound to tissue and does not circulate in the blood.

Special Populations: Race differences in digoxin pharmacokinetics have not been formally studied. Because digoxin is primarily eliminated as unchanged drug via the kidney and because there are no important differences in creatinine clearance among races, pharmacokinetic differences due to race are not expected.

The clearance of digoxin can be primarily correlated with renal function as indicated by creatinine clearance. The Cockcroft and Gault formula for estimation of creatinine clearance includes age, body weight, and gender. A table that provides the usual daily maintenance dose requirements of digoxin tablets based on creatinine clearance (per 70 kg) is presented in the DOSAGE AND ADMINISTRATION section.

Plasma digoxin concentration profiles in patients with acute hepatitis generally fell within the range of profiles in a group of healthy subjects.

Pharmacodynamic and Clinical Effects: The times to onset of pharmacologic effect and to peak effect of preparations of digoxin are shown in Table 2:

Table 2: Times to Onset of Pharmacologic Effect and to Peak Effect of Preparations of Digoxin

Product	Time to Onset of Effect*	Time to Peak Effect*
Digoxin Tablets	0.5-2 hours	2-6 hours
Digoxin Pediatric Elixir	0.5-2 hours	2-6 hours
Digoxin Solution in Capsules	0.5-2 hours	2-6 hours
Digoxin Injection/IV	5-30 minutes†	1-4 hours

*Documented for ventricular response rate in atrial fibrillation, inotropic effects and electrocardiographic changes.
†Depending upon rate of infusion.

Hemodynamic effects: Digoxin produces hemodynamic improvement in patients with heart failure. Short- and long-term therapy with the drug increases cardiac output and lowers pulmonary artery pressure, pulmonary capillary wedge pressure, and systemic vascular resistance. These hemodynamic effects are accompanied by an increase in the left ventricular ejection fraction and a decrease in end-systolic and end-diastolic dimensions.

Chronic Heart Failure: Two 12-week, double-blind, placebo-controlled studies enrolled 178 (RADIANCE trial) and 88 (PROVED trial) patients with NYHA class II or III heart failure previously treated with digoxin, a diuretic, and an ACE inhibitor (RADIANCE only) and randomized them to placebo or treatment with digoxin. Both trials demonstrated better preservation of exercise capacity in patients randomized to digoxin. Continued treatment with digoxin reduced the risk of developing worsening heart failure, as evidenced by heart failure-related hospitalizations and emergency care and the need for concomitant heart failure therapy. The larger study also showed treatment-related benefits in NYHA class and patients' global assessment. In the smaller trial, these trended in favor of a treatment benefit.

The Digitalis Investigation Group (DIG) main trial was a multicenter, randomized, double-blind, placebo-controlled mortality study of 6,801 patients with heart failure and left ventricular ejection fraction ≤0.45. At randomization, 67% were NYHA class I or II, 71% had heart failure of ischemic etiology, 44% had been receiving digoxin, and most were receiving concomitant ACE inhibitor (94%) and diuretic (82%). Patients were randomized to placebo or digoxin, the dose of which was adjusted for the patient's age, sex, lean body weight, and serum creatinine (see DOSAGE AND ADMINISTRATION), and followed for up to 58 months (median 37 months). The median daily dose prescribed was 0.25 mg. Overall all-cause mortality was 35% with no difference between groups (95% confidence limits for relative risk of 0.91 to 1.07). Digoxin was associated with a 25% reduction in the number of hospitalizations for heart failure, a 28% reduction in the risk of a patient having at least one hospitalization for heart failure, and a 6.5% reduction in total hospitalizations (for any cause).

Use of digoxin was associated with a trend in reduction in time to all-cause death or hospitalization. The trend was evident in subgroups of patients with mild heart failure as well as more severe disease, as shown in Table 3. Although the effect on all-cause death or hospitalization was not statistically significant, much of the apparent benefit derived from effects on mortality and hospitalization attributed to heart failure.

Table 3: Subgroup Analyses of Mortality and Hospitalization During the First Two Years Following Randomization.

	n	Risk of All-Cause Mortality or All-Cause Hospitalization*		
		Placebo	Digoxin	Relative risk‡
All Patients (EF ≤ 0.45)	6801	604	593	0.94 (0.88-1.00)
NYHA I/II	4571	549	541	0.96 (0.89-1.04)
EF 0.25-0.45	4543	568	571	0.99 (0.91-1.07)
CTR ≤ 0.55	4455	561	563	0.98 (0.91-1.06)
NYHA III/IV	2224	719	696	0.88 (0.80-0.97)
EF < 0.25	2258	677	637	0.84 (0.76-0.93)
CTR > 0.55	2346	687	650	0.85 (0.77-0.94)
EF > 0.45†	987	571	5[illegible]	1.04 (0.88-1.23)

	n	Risk of HF-Related Mortality or HF-Related Hospitalization*		
		Placebo	Digoxin	Relative risk‡
All Patients (EF ≤ 0.45)	6801	294	217	0.69 (0.63-0.76)
NYHA I/II	4571	242	178	0.70 (0.62-0.80)
EF 0.25-0.45	4543	244	190	0.74 (0.66-0.84)
CTR ≤ 0.55	4455	239	180	0.71 (0.63-0.81)
NYHA III/IV	2224	402	295	0.65 (0.57-0.75)
EF < 0.25	2258	394	270	0.61 (0.53-0.71)
CTR > 0.55	2346	398	287	0.65 (0.57-0.75)
EF > 0.45†	987	179	136	0.72 (0.53-0.99)

*Number of patients with an event during the first 2 years per 1000 randomized patients.
†Relative risk (95% confidence interval).
‡DIG Ancillary Study.

In situations where there is no statistically significant benefit of treatment evident from a trial's primary endpoint, results pertaining to a secondary end-point should be interpreted cautiously.

Chronic Atrial Fibrillation: In patients with chronic atrial fibrillation, digoxin slows rapid ventricular response rate in linear dose-response fashion from 0.25 to 0.75 mg/day. Digoxin should not be used for the treatment of multifocal atrial tachycardia.

INDICATIONS AND USAGE:

Heart Failure: DIGITEK is indicated for the treatment of mild to moderate heart failure. Digoxin increases left ventricular ejection fraction and improves heart failure symptoms as evidenced by exercise capacity and heart failure-related hospitalizations and emergency care, while having no effect on mortality. Where possible, digoxin should be used with a diuretic and an angiotensin-converting enzyme inhibitor, but an optimal order for starting these three drugs cannot be specified.

Atrial Fibrillation: DIGITEK is indicated for the control of ventricular response rate in patients with chronic atrial fibrillation.

CONTRAINDICATIONS: Digitalis glycosides are contraindicated in patients with ventricular fibrillation or in patients with a known hypersensitivity to digoxin. A hypersensitivity reaction to other digitalis preparations usually constitutes a contraindication to digoxin.

WARNINGS:

Sinus Node Disease and AV Block: Because digoxin slows sinoatrial and AV conduction, the drug commonly prolongs the PR interval. The drug may cause severe sinus bradycardia or sinoatrial block in patients with pre-existing sinus node disease and may cause advanced or complete heart block in patients with pre-existing incomplete AV block. In such patients consideration should be given to the insertion of a pacemaker before treatment with digoxin.

Accessory AV Pathway (Wolff-Parkinson-White Syndrome): After intravenous digoxin therapy, some patients with paroxysmal atrial fibrillation or flutter and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway bypassing the AV node, leading to a very rapid ventricular response or ventricular fibrillation. Unless conduction down the accessory pathway has been blocked (either pharmacologically or by surgery), digoxin should not be used in such patients. The treatment of paroxysmal supraventricular tachycardia in such patients is usually direct-current cardioversion.

Use in Patients with Preserved Left Ventricular Systolic Function: Patients with certain disorders involving heart failure associated with preserved left ventricular ejection fraction may be particularly susceptible to toxicity of the drug. Such disorders include restrictive cardiomyopathy, constrictive pericarditis, amyloid heart disease, and acute cor pulmonale. Patients with idiopathic hypertrophic subaortic stenosis may have worsening of the outflow obstruction due to the inotropic effects of digoxin.

PRECAUTIONS:

Use in Patients with Impaired Renal Function: Digoxin is primarily excreted by the kidneys; therefore, patients with impaired renal function require smaller than usual maintenance doses of digoxin (see DOSAGE AND ADMINISTRATION). Because of the prolonged elimination half-life, a longer period of time is required to achieve an initial or new steady-state serum concentration in patients with renal impairment than in patients with normal renal function. If appropriate care is not taken to reduce the dose of digoxin, such patients are at high risk for toxicity, and toxic effects will last longer in such patients than in patients with normal renal function.

Use in Patients with Electrolyte Disorders: In patients with hypokalemia or hypomagnesemia, toxicity may occur despite serum digoxin concentrations below 2 ng/mL, because potassium or magnesium depletion sensitizes the myocardium to digoxin. Therefore, it is desirable to maintain normal serum potassium and magnesium concentrations in patients being treated with digoxin. Deficiencies of these electrolytes may result from malnutrition, diarrhea, or prolonged vomiting, as well as the use of the following drugs or procedures: diuretics, amphotericin B, corticosteroids, antacids, dialysis, and mechanical suction of gastrointestinal secretions.

Hypercalcemia from any cause predisposes the patient to digitalis toxicity. Calcium, particularly when administered rapidly by the intravenous route, may produce serious arrhythmias in digitalized patients. On the other hand, hypocalcemia can nullify the effects of digoxin in humans; thus, digoxin may be ineffective until serum calcium is restored to normal. These interactions are related to the fact that digoxin affects contractility and excitability of the heart in a manner similar to that of calcium.

Use in Thyroid Disorders and Hypermetabolic States: Hypothyroidism may reduce the requirements for digoxin. Heart failure and/or atrial arrhythmias resulting from hypermetabolic or hyperdynamic states (e.g., hyperthyroidism, hypoxia, or arteriovenous shunt) are best treated by addressing the underlying condition. Atrial arrhythmias associated with hypermetabolic states are particularly resistant to digoxin treatment. Care must be taken to avoid toxicity if digoxin is used.

Use in Patients with Acute Myocardial Infarction: Digoxin should be used with caution in patients with acute myocardial infarction. The use of inotropic drugs in some patients in this setting may result in undesirable increases in myocardial oxygen demand and ischemia.

Use During Electrical Cardioversion: It may be desirable to reduce the dose of digoxin for 1 to 2 days prior to electrical cardioversion of atrial fibrillation to avoid the induction of ventricular arrhythmias, but physicians must consider the consequences of increasing the ventricular response if digoxin is withdrawn. If digitalis toxicity is suspected, elective cardioversion should be delayed. If it is not prudent to delay cardioversion, the lowest possible energy level should be selected to avoid provoking ventricular arrhythmias.

Laboratory Test Monitoring: Patients receiving digoxin should have their serum electrolytes and renal function (serum creatinine concentrations) assessed periodically; the frequency of assessments will depend on the clinical setting. For discussion of serum digoxin concentrations, see DOSAGE AND ADMINISTRATION section.

Drug Interactions: Potassium-depleting *diuretics* are a major contributing factor to digitalis toxicity. *Calcium*, particularly if administered rapidly by the intravenous route, may produce serious arrhythmias in digitalized patients. *Quinidine, verapamil, amiodarone, propafenone, indomethacin, itraconazole, alprazolam,* and *spironolactone* raise the serum digoxin concentration due to a reduction in clearance and/or in volume of distribution of the drug, with the implication that digitalis intoxication may result. *Erythromycin* and *clarithromycin* (and possibly other *macrolide antibiotics*) and *tetracycline* may increase digoxin absorption in patients who inactivate digoxin by bacterial metabolism in the lower intestine, so that digitalis intoxication may result (see CLINICAL PHARMACOLOGY: Absorption). *Propantheline* and *diphenoxylate*, by decreasing gut motility, may increase digoxin absorption. *Antacids, kaolin-pectin, sulfasalazine, neomycin, cholestyramine,* certain *anticancer drugs,* and *metoclopramide* may interfere with intestinal digoxin absorption, resulting in unexpectedly low serum concentrations. *Rifampin* may decrease serum digoxin concentration, especially in patients with renal dysfunction, by increasing the nonrenal clearance of digoxin. There have been inconsistent reports regarding the effects of other drugs [e.g., *quinine, penicillamine*] on serum digoxin concentration. *Thyroid* administration to a digitalized, hypothyroid patient may increase the dose requirement of digoxin. Concomitant use of digoxin and *sympathomimetics* increases the risk of cardiac arrhythmias. *Succinylcholine* may cause a sudden extrusion of potassium from muscle cells, and may thereby cause arrhythmias in digitalized patients. Although beta-adrenergic blockers or calcium channel blockers and digoxin may be useful in combination to control atrial fibrillation, their additive effects on AV node conduction can result in advanced or complete heart block.

Due to the considerable variability of these interactions, the dosage of digoxin should be individualized when patients receive these medications concurrently. Furthermore, caution should be exercised when combining digoxin with any drug that may cause a significant deterioration in renal function, since a decline in glomerular filtration or tubular secretion may impair the excretion of digoxin.

Drug/Laboratory Test Interactions: The use of therapeutic doses of digoxin may cause prolongation of the PR interval and depression of the ST segment on the electrocardiogram. Digoxin may produce false positive ST-T changes on the electrocardiogram during exercise testing. These electrophysiologic effects reflect an expected effect of the drug and are not indicative of toxicity.

Carcinogenesis, Mutagenesis, Impairment of Fertility: There have been no long-term studies performed in animals to evalu[illegible] genic potential, nor have studies been conducte[illegible] genic potential of digoxin or its potential to aff[illegible]

Pregnancy: ***Teratogenic Effects:*** Pregnancy C[illegible] Animal